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BRITISH MEDICAL JOURNAL

LONDON SATURDAY DECEMBER 13 1947

PREVENTION OF RENAL DAMAGE BY USE OF MIXTURES OF SULPHONAMIDES*

ANIMAL-EXPERIMENTAL AND CLINICAL STUDIES

BY

DAVID LEHR, M.D.†

Assistant Professor, Department of Medicine and Pharmacology, New York Medical College; Assistant Attending Physician, Flower and Fifth Avenue Hospitals, New York City

A new and simple approach to the prevention of concrement formation in the urinary tract caused by sulphonamides emerged from the observation that a saturated aqueous or urinary solution of one derivative of sulphanilamide could still be fully saturated with a second and third sulphonamide even if only of slightly different molecular structure, each of the compounds behaving as though it were present alone and exerting no influence on the solubility of the others. Consequently, in solutions containing several sulphonamides the maximum obtainable concentration appeared expressed by the additive solubilities of all individual drugs present (Lehr, 1945). This principle is illustrated in diagrammatic form in Fig. 1.

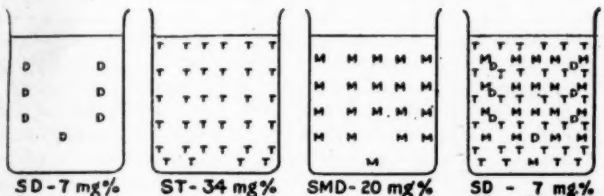

FIG. 1.—Diagram illustrating the individual and combined solubilities of sulphadiazine (SD), sulphathiazole (ST), and sulphamerazine (SMD) in water at room temperature (20° C.).

The figure elucidates the theoretical explanation of the phenomenon—namely, the specifically different molecular distribution in space of chemically different compounds. It also makes it clear that precipitation due to oversaturation will not occur more readily in the solution containing three sulphonamides, with a total concentration of 61 mg. per 100 ml., than in any one of the three individual solutions, with necessarily much lower maximum sulphonamide levels. Hence, at *equal* total sulphonamide concentrations the danger of precipitation will be significantly smaller in solutions of sulphonamide mixtures; it follows, in addition, that any increase in the number of components comprising a sulphonamide mixture will further diminish the chances of precipitation.

It was reasoned on the basis of this observation that the danger of the formation of sulphonamide crystals in the renal tubules could be considerably reduced by employing combinations of *partial* dosages of two or three therapeutically equivalent sulphonamides rather than the *full* dosage of any one single compound. Actually the hazard of precipitation from such combinations should be only as great as if each sulphonamide had been administered alone and in the partial dosage contained in the mixture

Results of Animal Experimental Studies

Comparative studies of the toxicity and of the absorption and excretion of sulphonamide mixtures and their individual constituents were carried out on 750 albino rats from our own standard colony (Lehr, 1945, 1947). A condensation of the most important findings is presented in the accompanying tables and figures.

1. Acute Toxicity

Table I illustrates the values for the acute toxicity. It demonstrates that combinations of sulphonamides are significantly less toxic than comparable or equal amounts of their individual constituents. Estimation on the basis of the toxicity figures of the separate compounds would give, for example, an expected toxicity of about 77% for the sulphathiazole–sulphadiazine mixture, about 68% for the sulphamerazine—sulphadiazine combination, and about 74% for the mixture of sulphadiazine and sulphapyridine, whereas the actual values derived from experimental results were only 12%, 37%, and 0 respectively.

TABLE I.—*Acute Toxicity of Sulphonamides given Singly and in Various Combinations. (Single Intraperitoneal Injection of Sodium Salts in Albino Rats)*

Drug	Dose (g./kg.)		No. of Animals	Deaths
	Partial	Total		
Sulphadiazine		1·5	90	85%
Sulphthiazole		1·1	25	65%
Sulphamerazine		1·5	29	52%
Sulphapyridine		1·1	35	63%
Sulphapyrazine		1·3	17	77%
Sulphadiazine + Sulphathiazole	0·75 + 0·55	1·3	60	12%
Sulphadiazine + Sulphamerazine	0·75 + 0·75	1·5	30	37%
Sulphadiazine + Sulphapyridine	0·75 + 0·55	1·3	16	0
Sulphadiazine + Sulphathiazole + Sulphamerazine	0·54 + 0·42 + 0·54	1·5	40	0
Sulphadiazine + Sulphapyridine + Sulphamerazine	0·54 + 0·42 + 0·54	1·5	10	0
Sulphadiazine + Sulphapyrazine + Sulphamerazine	0·54 + 0·42 + 0·54	1·5	10	0

*Read at the Seventeenth International Physiological Congress in Oxford, on July 23, 1947.

†This investigation has been aided by grants from the Josiah Macy Jr. Foundation, New York City, and the Schering Corporation, Bloomfield, N.J.

Mixtures of *three* sulphonamides proved completely non-toxic at the 1.5 g. per kg. total dose level. This remarkably low toxicity pointed to a further increase in the protection afforded to the kidney against blockage with sulphonamide crystals.

Evidence of the presence or absence of renal obstruction was obtained from post-mortem examinations of the kidneys. Various degrees of kidney block caused by deposits of sulphonamide crystals in the renal tubules were observed in all animals succumbing to treatment with any of the five sulphonamides given singly. The kidneys appeared greatly enlarged and oedematous, and contained crystalline plugs in the papillary ducts, which in severe cases fanned out into the cortex. These drug deposits were clearly visible to the naked eye and easily demonstrable under the microscope. Rats treated with mixtures of three sulphonamides showed complete absence of renal blockage, and hence had normal kidneys. The lack of renal obstruction could also be inferred from normal non-protein nitrogen levels in the blood and high urinary elimination figures of sulphonamide. Added proof was derived from accurate chemical determinations of the sulphonamide amounts in the kidneys at various intervals after intraperitoneal injection of single and mixed sulphonamides.

Fig. 2 summarizes one representative experiment with animal groups killed 24 hours after intraperitoneal injection of sulphadiazine, sulphathiazole, sulphamerazine, and their combination

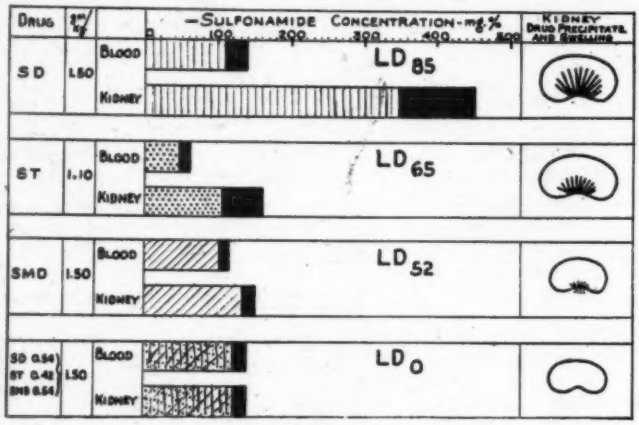

FIG. 2.—Findings in blood and kidneys of albino rats 24 hours after intraperitoneal injection of sulphadiazine (SD), sulphathiazole (ST), and sulphamerazine (SMD), given singly and in combination.

in the dosages used in the acute toxicity study. It indicates that rats injected with sulphadiazine showed the greatest discrepancy between blood and renal concentration of sulphonamide. The excessive concentration of sulphadiazine in the kidney is readily explainable on the basis of the massive crystalline deposition observed in this organ. The findings were similar although less marked in the sulphathiazole group. However, in this instance the large amount of conjugated sulphathiazole in the kidneys was of particular importance since the acetylated product has a solubility of only 7 mg. per 100 ml. at body temperature. Sulphamerazine caused the least intratubular precipitation, but showed the greatest tendency to the formation of gravel and concrements in the renal pelves and ureters.

The mixture of all three sulphonamides did not produce any concrement formation in the urinary tract, and hence also did not reveal any difference between the concentration of sulphonamide in the blood and in the kidneys. It seems highly significant that the blood level of free sulphonamide resulting from the non-toxic dose of the mixture was actually higher than the levels obtained with comparable though fatal dosages of any *one* of the three mixture components under the conditions of renal impairment.

2. Subacute and Chronic Toxicity

The results of studies on the subacute toxicity are summarized in Table II. The daily dose of sulphonamides used was 0.9 g. per kg. In the mixture groups it consisted of equal amounts of the two or three compounds. The mortality figures shown

TABLE II.—*Subacute Toxicity of Sulphonamides given Singly and in Various Combinations. (Intraperitoneal Injection of Sodium Salts for 5 Consecutive Days in Albino Rats)*

Drug	Dose (g./kg.)		No of Animals	Deaths
	Partial	Total		
Sulphadiazine		0·9	25	100%
Sulphathiazole		0·9	15	100%
Sulphamerazine		0·9	20	75%
Sulphapyrazine		0·9	10	100%
Sulphapyridine		0·9	15	94%
Sulphadiazine	0·45	0·9	10	40%
Sulphathiazole	0·45			
Sulphadiazine	0·45	0·9	10	40%
Sulphamerazine	0·45			
Sulphadiazine	0·3	0·9	10	0
Sulphamerazine	0·3			
Sulphathiazole	0·3			
Sulphadiazine	0·3	0·9	10	0
Sulphamerazine	0·3			
Sulphapyridine	0·3			
Sulphadiazine	0·3	0·9	10	0
Sulphamerazine	0·3			
Sulphapyrazine	0·3			

are those observed on the sixth day of the experiment. The strikingly low toxicity of combinations as compared with the high mortality from separate compounds is immediately apparent. It should be mentioned, for the sake of completeness, that studies were also carried out with various mixtures containing *sulphacetamide* (N_1-acetylsulphanilamide), a sulphonamide of relatively high solubility. They proved, as expected, that the toxicity of such combinations was particularly low.

The results of the acute and subacute studies were confirmed in part also in chronic feeding experiments with weanling albino rats, although in tests based on voluntary drug intake the results are of necessity less clear-cut. On the one hand the taste of the standard food seems to be spoiled by certain sulphonamides (sulphathiazole, sulphamerazine) and not by others (sulphadiazine), which results in great differences in the food intake. On the other hand, tolerable amounts ingested over a long period of time may be insufficient to produce fatal renal complications but high enough to result in serious reactions due to the tissue toxicity of the sulphonamides. Hence, for comparative investigations of the *renal* toxicity of sulphonamides and their mixtures the incorporation of the drugs into standard food for *voluntary* consumption is not a good procedure.

3. Absorption-Excretion

The comparative absorption from the peritoneal cavity is exemplified for three combinations with the dosages used in the evaluation of acute toxicity. Fig. 3 shows that the blood levels from the sulphathiazole–sulphadiazine mixture are at all times almost as high as from sulphadiazine alone, despite the low toxicity of this combination. The urine volumes indicate an unimpeded flow of urine in the rats treated with the mixture; this group consequently also reveals by far the highest values for urinary drug excretion.

In a similar manner Fig. 4 demonstrates that the blood levels and particularly the urine concentrations of the sulphamerazine–sulphadiazine combination are higher than expected on the basis of the values from the individual compounds. It is evident, in addition, from the columns representing total urinary elimination of the drugs (in this instance on a cumulative basis) that excretion of the mixture is far more complete than from either compound administered singly in equal amounts.

Fig. 5 illustrates the absorption and excretion of the mixture of *three* compounds. If compared with the previous two figures it is apparent that this sulphonamide combination gives excellent blood and urine concentrations. The total urinary elimination of sulphonamides is not only higher than from any *one* of the three compounds administered *singly*, but also significantly more complete than from a mixture of two. The same behaviour of sulphonamide mixtures was observed also with small dosages and from other routes of administration.

The fate of sulphonamides and their combinations after *oral* administration of *sublethal* amounts is depicted in a representative experiment with the sodium salts of sulphadiazine and

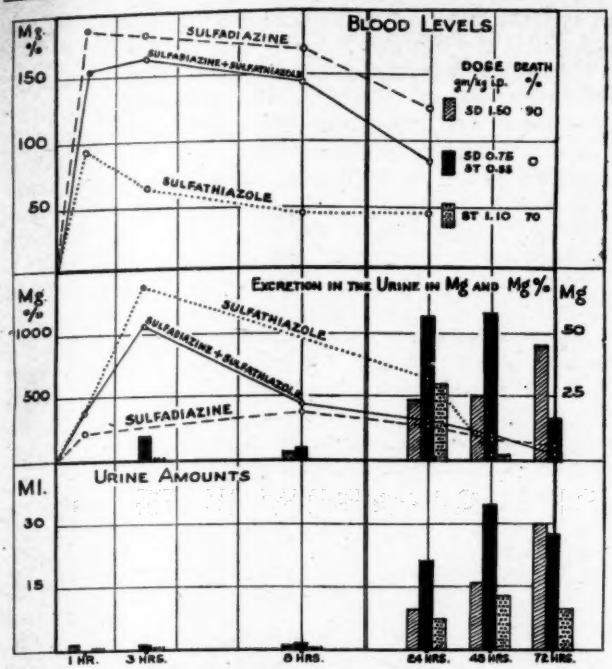

FIG. 3.—The absorption and excretion of sulphadiazine, sulphathiazole, and their combination in albino rats after intraperitoneal injection of single dosages. All figures represent the mean of the values of 10 animals.

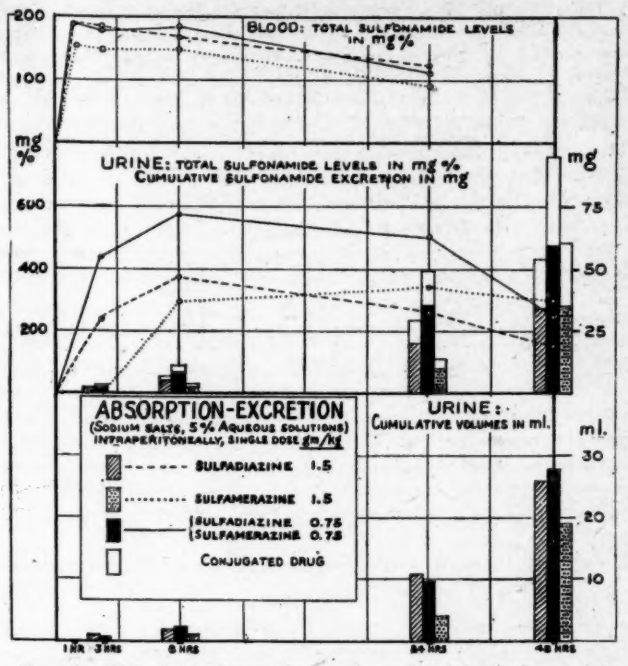

FIG. 4.—The absorption and excretion of sulphadiazine, sulphamerazine, and their combination in albino rats after intraperitoneal injection of single dosages. All figures represent the mean of the values of 10 animals.

sulphathiazole. Fig. 6 illustrates the absorption and excretion after intubation of 1 g. of the mixture per kg. of body weight as compared with the same weight amounts of the separate compounds. It is apparent from the graph that the mixture gives the highest blood levels, initially also the highest urine levels, and again by far the most complete urinary excretion, indicating that *a combination of half dosages* is *more fully utilized* than the same amount of either sulphadiazine or sulphathiazole.

The explanation for the more complete absorption and elimination of sulphonamide combinations emerged from tests with single drugs in the partial dosages contained in the mixture. These studies proved that smaller amounts are more completely absorbed from the gut, and consequently also more completely eliminated by the kidney. This behaviour remained apparently unchanged even if two sulphonamides were administered simultaneously. Hence, with regard to absorption and excretion, the body seems to handle a combination of sulphonamides as if each of its constituents were present alone and in the partial dosage contained in the mixture.

Table III illustrates this general principle in the renal excretion figures for the sulphathiazole–sulphadiazine mixture as

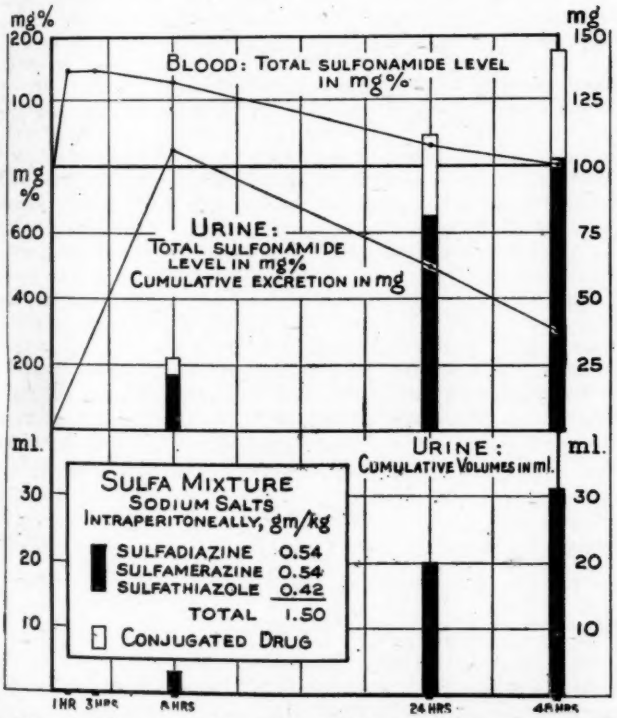

FIG. 5.—The absorption and excretion of a mixture containing partial dosages of sulphadiazine, sulphamerazine, and sulphathiazole after intraperitoneal injection of a single dose. All figures represent the mean of the values of 10 animals.

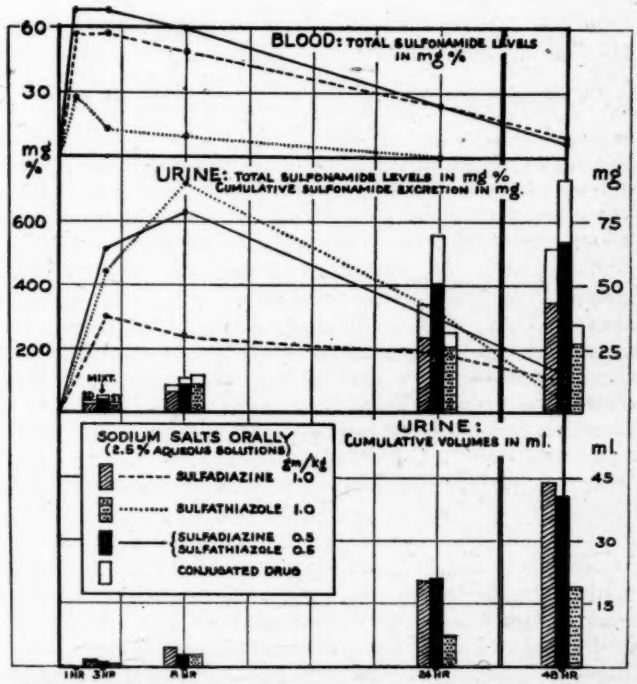

FIG. 6.—The absorption and excretion of sulphadiazine, sulphathiazole, and their combination after a single oral intubation. All figures represent the mean of the values of 10 animals.

contrasted with the values for the single compounds in equal and half dosages (Fig. 6). It is clearly apparent that the percentage of urinary excretion is strikingly higher from *half*

TABLE III.—*The Renal Elimination after 24 Hours of Sulphadiazine and Sulphathiazole, given Singly and in Combination. (Administration of Sodium Salts by Stomach Tube to Groups of 10 Albino Rats)*

Drug	Amount in g./kg. Body Weight		Amount of Dose Excreted
	Administered	Excreted	
Sulphadiazine	0·5	0·210	42%
	1·0	0·270	27%
Sulphathiazole ..	0·5	0·175	35%
	1·0	0·200	20%
Sulphadiazine	0·5	0·440	44%
Sulphathiazole	0·5		

dosages, whether given singly or in combinations. Incidentally, the observations in the laboratory animal that sulphonamide mixtures give good therapeutic blood and urine levels were fully confirmed in absorption–excretion studies in man.

Results of In-vitro Antibacterial Activity of Sulphonamide Mixtures

The main result of *in-vitro* experiments on antibacterial activity of sulphonamide mixtures was the observation that the action of similarly effective sulphonamides in combinations corresponds largely to the *total* content of sulphonamide; in other words, in mixtures of different but similarly effective sulphonamides the bacteriostatic effect is generally additive. True potentiation of action was observed in some instances (Lehr, 1945).

It should be kept in mind, however, that these results were obtained with equal sulphonamide concentrations in the test-tube, whereas the administration of equal dosages of the different sulphonamides and their combinations would result in significant differences in the drug concentrations in blood and tissues. In accordance with the results of the absorption-excretion studies, mixtures give excellent tissue levels; hence they should prove *in vivo* at least of the same, if not of higher, antibacterial value if compared with equal dosages of any one of their individual components. This point of view was well supported by *clinical results.*

Results of the Therapeutic Use of Sulphonamide Combinations

Up to the present a total of more than 700 unselected patients with systemic infections have been treated at the Flower and Fifth Avenue Hospitals and at the Metropolitan Hospital in New York City with a mixture containing equal amounts of sulphathiazole and sulphadiazine, or sulphadiazine and sulphamerazine, on a routine dosage schedule (Lehr, 1946; Lehr *et al.*, 1946). The oral route was used in the majority of cases. In children the sulphadiazine–sulphamerazine combination was also given by the subcutaneous route. These results will be published later. Adequate fluid intake was assured, but no alkalizing agents were employed.

The therapeutic response to both sulphonamide combinations was highly satisfactory in most instances. Defervescence and general clinical improvement seemed to occur with greater speed when compared with previous experience with any of the drugs administered separately. Hence the total amount of sulphonamide used was comparatively small. Therapeutically effective blood levels (5 to 20 mg. free sulphonamide per 100 ml.) were maintained with ease. Urinary concentrations of sulphonamide varied between 100 and 600 mg. per 100 ml. Conjugation figures were as a rule low, ranging between 3 and 20% of the total level in the blood, and 10 and 40% of the total amount in the urine.

Crystalluria was infrequent, and never of the "massive" type observed so commonly during therapy with single compounds. Of more than 900 acid morning specimens of urine containing sulphonamide mixtures which were examined under the microscope after sharp centrifugation only about 7% were found to hold moderate or small amounts of sulphonamide crystals, as contrasted with the incidence of crystalluria of 29% from sulphadiazine, 26% from sulphamerazine, and 70% from sulphathiazole alone (Flippin *et al.*, 1941; Flippin and Reinhold, 1946). None of the patients treated with mixtures developed any sign of serious renal irritation. Quite unexpectedly the incidence of allergic reactions also seemed to have decreased. Nausea and vomiting were rare. No other toxic reactions were encountered. At present we are engaged in clinical studies with various mixtures of three sulphonamides.

Confirmation of these investigations came recently from several sources. Whitehead (1946), at the University of Colorado, confirmed the animal experimental data. Flippin and Reinhold (1946), at the University of Pennsylvania, extended the clinical observations. They showed in a well-controlled study that "the use of sulphadiazine and sulphamerazine in mixtures containing equal parts of each drug led to a considerably decreased incidence of crystalluria compared with that observed when either compound was administered singly." They concluded that for the prevention of crystalluria the use of the mixture was as effective as the administration of sodium bicarbonate at the rate of 12 g. a day with either sulphadiazine or sulphamerazine. Finally, Hagerman and his co-workers (Frisk *et al.*, 1946, 1947), in Sweden, using a combination of sulphathiazole, sulphadiazine, and sulphamerazine, arrived independently at confirmatory animal-experimental and clinical results.

Summary

A new and simple approach to the prevention of renal complications from sulphonamide therapy is presented. It consists in the use of a *mixture* of several sulphonamides in partial dosages instead of single compounds. In solution each sulphonamide component of the mixture behaves as if present alone, exerting no influence on the solubility of the others. Consequently the danger of drug precipitation in the kidney was significantly decreased with sulphonamide mixtures, as shown in animal experimental and clinical studies. Actually it was only as great as if each compound had been given alone and in the partial dosage contained in the combination. On the other hand the chemotherapeutic effect of these mixtures was roughly proportional to their total sulphonamide content.

The results of these studies indicate that combinations of two or more sulphonamides should be used in preference to single compounds for all indications, since they combine a high therapeutic efficacy with a remarkably low renal toxicity.

The principle of dissolving several structurally similar and therapeutically equivalent drugs in the same medium to the full extent of the separate saturation levels for each compound might prove of value in any instance where sparingly soluble drugs have to be incorporated into small volumes of solvent.

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SULPHAMERAZINE TREATMENT OF PNEUMONIA IN ADULTS

BY

HORACE JOULES, M.D., F.R.C.P.

AND

S. D. V. WELLER, M.D., M.R.C.P.

(From the Central Middlesex County Hospital)

Pneumonia lost many of its terrors with the discovery and development of the sulphonamides, and the results of treatment of this disease are progressively improving. There is, however, a tendency to regard the sulphonamide drugs as superseded by penicillin not only in the severely ill but even in mild conditions where the former have proved adequate. Needles are never pleasant to the patient or convenient to the attendant. We hope to show that sulphonamide treatment for primary pneumonia in adults is satisfactory in the vast majority of cases, and should be given before confirmation of a clinical diagnosis, in the form of bacteriological and radiological reports, is available. Further, we feel that all but the most severe cases in aged or debilitated patients are reduced by this treatment to a two-day fever which can be adequately treated at home. Hospital care, with facilities for fuller investigation and treatment, is needed only for patients who fail to respond rapidly to sulphonamides or who are critically ill or whose condition is otherwise complicated.

Pneumonia commonly occurs without the classical physical signs. We maintain that, in the absence of an influenzal epidemic, patients complaining of respiratory symptoms are suffering from some measure of lung consolidation if they have a temperature higher than 100° F. (37.8° C.) for more than one day. We have encountered many such patients in whom skiagrams have shown segmental or central consolidation, and we consider that all these cases should be given the benefit of a full course of a suitable sulphonamide without delay.

It is very desirable to obtain at the outset, and before treatment is started, a specimen of sputum for complete bacteriological investigation. This will give a reliable indication of the causal organism in 70% of cases. Radiological confirmation that resolution is complete, particularly in every patient over 40, is essential. Patients with carcinoma of the bronchus not infrequently present with pneumonia, but complete clearing rarely occurs.

Sulphamerazine

We do not attempt to prove that any sulphonamide is more successful than penicillin in the treatment of pneumonia (although we have reached this conclusion from a small series of cases that are not statistically significant). Sulphonamide therapy is certainly less troublesome, and with the newer preparations there is no need for frequent dosage, with consequent loss of sleep. Toxic effects are minimal. In this hospital patients may be admitted to any medical ward under the care of any of the physicians, so that treatment is that considered best by the physician concerned and is in no way standardized. By common consent, however, the treatment now used almost invariably is that with sulphamerazine.

Workers in America have compared the pharmacological properties of sulphamerazine with those of other sulphonamides (Hageman *et al.*, 1943 ; Schmidt *et al.*, 1944b), while its toxic effects have been compared with those of sulphadiazine by Dowling *et al.* (1944) and with those of sulphamezathine by Schmidt, Hughes, *et al.* (1944a). Reviews and clinical evaluations of the use of sulphamerazine in pneumonia have been published by Genecin and Nelson (1945), Heffner (1945), and Volini *et al.* (1945).

Sulphamerazine, a methyl homologue of sulphadiazine, is absorbed more rapidly and excreted more slowly than sulphadiazine. At equal blood levels it is no more toxic than sulphadiazine and is far less so than many of the older preparations. As a result, a single dose of sulphamerazine will produce a higher blood level of the drug, and more quickly, than the same dose of sulphadiazine, and this blood level will be longer maintained (Flippin, Reinold, and Gefter, 1943 ; *Medical Uses of Sulphonamides*, H.M.S.O., 1945 ; *Lancet*, 1943). Being more soluble than sulphadiazine it presents less risk of urinary obstruction with crystals (Anderson, Oliver, and Keefer, 1944). The rapid absorption renders parenteral administration almost unnecessary, since an oral dose will produce therapeutic blood levels in two hours, while within four hours the blood levels remain the same as those obtained by equal intravenous dosage (Murphy, Clark, and Flippin, 1943). Thus in comparison with older sulphonamides smaller doses of sulphamerazine less frequently given will produce and maintain an adequate blood level (12–15 mg. per 100 ml. of blood). The course we have found satisfactory consists of an initial "loading" dose of 3 g., followed in eight hours by 2 g. and then 1 g. eight-hourly. The doses can be arranged so that patient and attendant can have an uninterrupted night. With this regime a blood level of 15 mg. is reached within four hours (Welch, Mattis, Latven, Benson, and Shiels, 1943). We have found that this level is well maintained throughout treatment. Adequate urinary output must be maintained by giving six pints (3.4 litres) of fluid daily, but alkali is not required, since it decreases tubular reabsorption of the drug and therefore increases its loss by excretion.

In our experience the above dosage is always well tolerated and rapid subjective improvement occurs. The temperature falls to normal in 24 to 36 hours in most cases and never rises more than 1° F. above normal afterwards. Treatment is continued, according to the severity of the case, for 48 to 72 hours after the temperature has reached normal, so that a moderately severe case will need about five days' treatment (18 g. in all). We found no evidence that such a dosage produced a reduction in granulocytes in the blood that could be attributed to the drug. This agrees with the findings of others, using somewhat larger doses (Flippin, Gefter, Domm, and Clark, 1943). Most patients are fit to get up after a week and leave hospital between the tenth and the fourteenth day from admission. Breathing exercises from the day after the temperature has fallen accelerate the disappearance of added sounds in the lungs. Fig. 1 graphically represents the progress of a typical case.

In addition to specific drug therapy we find that adequate sleep on the first night of treatment is best obtained with an injection of 1/4 gr. (16 mg.) of morphine, which also suppresses the painful cough ; in older subjects pethidine, 100 mg. by injection, is adequate and in many ways preferable. A linctus for the first two or three days may be helpful to control the cough ; a really effective preparation, such as linctus heroin, should be used. Alternatively, 1/12 gr. (5.4 mg.) or 1/6 gr. (11 mg.) of "dicodid," by mouth, is satisfactory. Pleural pain rarely persists long after the start of sulphamerazine, and is well relieved by spraying the chest wall with ethyl chloride ; the relief lasts about three hours, and the spray may then be repeated if necessary. We have never resorted to strapping the chest.

Although the illness is shorter and less severe as a result of treatment, full convalescence is essential, since pneumonia affects predominantly those subject to the stresses

of overwork and the risks of overcrowding, and rarely strikes the healthy adult. The patient should be advised to see that his future life is modified so as to avoid a recurrence of those circumstances that rendered him an easier victim to pneumonia. This may mean that a housewife must be advised not to add to her burden by long hours in a factory and the enthusiastic gardener warned against over-indulgence in his hobby.

We have found that a small spike of temperature, up to but rarely exceeding 99.4° F. (37.4° C.), occurs in many cases. This spike was seen in 60% of our successfully treated cases, being found more often where a four-hourly temperature chart was maintained than where the temperature was taken twice daily. The spike occurred most frequently about thirty-six hours after the temperature had settled, and some cases showed two or more such spikes. In no instance was this phenomenon correlated with any

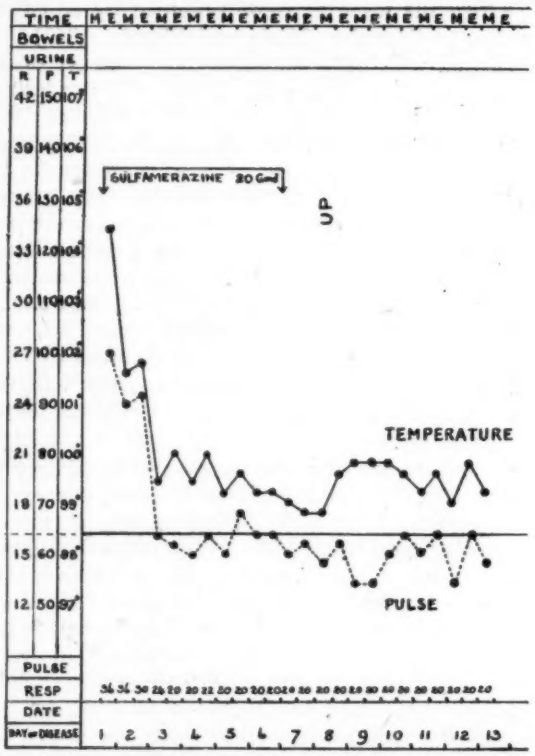

FIG. 1.—Chart of a typical case of severe lobar pneumonia treated with sulphamerazine.

failure of treatment or the development of any complication. It is met with as often in patients under penicillin as under sulphonamide therapy, and we have come to the conclusion that it need cause no misgiving.

Present Series

For this investigation the last 189 proved cases of pneumonia were studied—that is, those occurring since sulphamerazine became easily available. Criteria of diagnosis are clinical signs, supported by radiological evidence of well-defined consolidation, together with (in most cases) the presence of leucocytosis and the isolation of a causal micro-organism. Cases in which the pneumonia occurred as a terminal event in another mortal illness are excluded. In the series there were 101 males and 88 females. The average age for males was 43.0 years and for females 40.5 years, the extremes of age being 13 and 76 years.

Of these 189, 113 were treated with sulphamerazine from the start without a single death; 36 were treated with sulphamezathine (sulphadimethylpyrimidine), with three deaths; and 22 with penicillin, with one death. Combined treatment was given to 12 patients, one of whom died. The remaining cases were so mild that no specific therapy was deemed necessary. The details of those dying in these series are:

Treated with Sulphamezathine Alone (36 cases, 3 deaths)

1. Man aged 52.—Chronic bronchitis for seven years. History indefinite. Died within two hours of admission. Diagnosis at necropsy: left lower-lobe pneumonia.

2. Man aged 65.—An alcoholic polycythaemic patient. Indefinite chest illness for one month. Severe symptoms for three days. Died within 24 hours of admission. Diagnosis at necropsy: right mid-lobe pneumonia.

3. Woman aged 66.—A known case of aortic stenosis. Fluid complicating right lower-lobe pneumonia. Collapsed three days before admission after nursing dying husband. Severely ill. No response to treatment. Diagnosis confirmed at necropsy.

Treated with Penicillin Alone (22 cases, 1 death)

4. Man aged 59.—Admitted with acute pulmonary oedema. Died within 12 hours of admission. Diagnosis at necropsy: rheumatic aortic stenosis, acute pulmonary oedema, left-sided pneumonia.

Treated with Combined Therapy (12 cases, 1 death)

5. Girl aged 15.—Died 12 hours after admission. Left lower-lobe pneumonia complicating rheumatic mitral stenosis and aortic regurgitation, associated with acute pulmonary oedema. Confirmed at post-mortem examination.

It will be seen that no therapy could offer much, if any, chance of recovery.

The Sulphamerazine Group

The sulphamerazine cases are considered in further detail. Three of the 113 were given sulphamerazine together with penicillin from the outset; one was critically ill, another less severely ill but rather old (66), and the third a case of moderate severity in a soldier, who would probably have responded well to either treatment alone. Among the remaining 110 patients the condition was classified as mild, moderate, or severe, according to the clinical impression. The age distribution, in decades, of these 110 patients is recorded in the following table.

Age Period	No. of Cases	Age Period	No. of Cases
13–20	11	51–60	17
21–30	22	61–70	11
31–40	25	Over 70	3
41–50	21		

Bacteriology

The sputa of 87 cases, in all groups of severity, were examined on admission, and 60 of these yielded on culture a causal micro-organism. The examination thus gave a positive finding in 70%. The pneumococcus was cultured in 53 cases, a haemolytic streptococcus in 10 cases (seven times we encountered both organisms); Friedländer's bacillus in 1 case, and *Staph. aureus* in 3 cases. Of the 27 cases which grew no pathogenic organisms the majority responded to treatment as if they had been pneumococcal in aetiology. Most cultures grew non-pathogenic organisms in addition, most frequently *Neisseria catarrhalis* and *Str. viridans*—the latter rarely in free or pure growth. This finding emphasizes the fact that to be of most value this examination must be carried out on a specimen of real sputum from the lung and not saliva. In young and non-smoking subjects a specimen may be unobtainable.

Results

There were 17 mild cases in the series—9 men (average age 38) and 8 women (average age 37); thus these patients were, on the whole, young. Treatment of all but one was totally successful, fever disappearing in an average of 1.4 days and the patients leaving hospital in 11 days. The average dosage of sulphamerazine was 16.5 g. and the success rate 94%.

The moderately ill patients numbered 59 (31 men and 28 women), the average ages being 40 and 43 respectively. In 50 cases the results were totally successful, the temperature reaching normal in two days and discharge occurring in 15 days on the average. The dosage of drug used was 19 g. and the success rate 85%.

Of the 34 patients classified as severe cases the average age was 42 for both sexes, there being 21 men and 13 women. Sulphamerazine produced a successful response in 27, with the pyrexia settling in 2.2 days and discharge being given in 16 days after an average dosage of 19 g. The success rate here is 79%.

Thus, of 110 patients treated with sulphamerazine when a clinical diagnosis was made 93 gave a response regarded therapeutically as successful—an overall success rate of 84.5%. All cases were followed up in the out-patient department after convalescence if clearing was not demonstrated radiologically before discharge.

Among the successful cases there were 10 which developed small amounts of sterile pleural effusion, and 3 which had relapses of fever responding to a further course of sulphamerazine. Other minor complications were one temporary lobar collapse, one femoral thrombosis, and one abortion. In no case was convalescence seriously delayed.

Cases Given Additional Treatment

In 17 cases the response was deemed inadequate and further treatment was given. Fluid developed in 5 cases in amounts sufficient to justify aspiration. The fluid remained sterile throughout and no empyema occurred in the series. Parenteral penicillin was given to each.

Two cases developed lobar collapse, for which penicillin was administered to prevent a new infection becoming established in the collapse area. One severely ill woman developed a confusional psychosis after 7 g. of the drug, which was stopped and penicillin substituted. Her confusion cleared rapidly and she left hospital on the fifteenth day, her progress delayed neither by her psychosis nor by a small sterile effusion which developed. One moderately ill man with a pneumococcal infection developed a drug fever. After a tendency to early settling his temperature rose again and remained high throughout a course of 20 g. of sulphamerazine, falling critically thereafter, having almost reached normal before a three-day course of penicillin was started—probably unnecessarily.

Six patients seemed refractory to sulphonamides. Three yielded a growth of pneumococci on sputum culture, though the growth was not free, and—unfortunately in the light of events—the drug resistance of these strains was not tested *in vitro*. One case was mild and the temperature subsided by very slow lysis over four weeks, apparently unaffected by sulphamerazine (18 g.) or penicillin (three-hourly for 14 days). The other two (one moderate, one severe) responded promptly to penicillin after sulphamerazine had failed. Two other cases produced no pathogenic organisms from the sputum, and both were severely ill. One responded slowly and became afebrile on the eighth day of treatment, which consisted of sulphamerazine 20 g., producing a short-lived response, together with penicillin from the third to the tenth day. The other gradually improved over nine weeks regardless of treatment, his progress being punctuated by thrombophlebitis at three weeks and a lung abscess in the affected lobe at six weeks. These complications cleared completely by four months from the onset of his illness. The sixth case had 40 g. of sulphapyridine during 28 days before admission, and 18 g. of sulphamerazine resulted in no improvement, but the condition yielded dramatically to penicillin.

Staphylococcal Pneumonia

The remaining two cases were due to *Staph. aureus*. Certain strains of staphylococci are moderately sensitive to sulphamerazine. There were three cases of staphylococcal pneumonia in this series; one case, that of a man of 70, was among those successfully treated. His fever had already subsided when the laboratory reported a pure growth of *Staph. aureus* from his sputum; no relapse occurred after treatment. In the other two progress was not so smooth. The first became afebrile in 36 hours, so treatment was not changed on the bacteriological findings; a relapse followed the end of treatment, and this was promptly and finally dealt with by penicillin (60,000 units three-hourly for seven days). The second case seems typical of this condition, and is described in more detail; the temperature, pulse, and respirations are reproduced in Fig. 2.

A man, aged 34, who had been overworking, was seized at 3.30 p.m. on June 3, 1946, with severe left chest pain, breathing becoming difficult. He sweated profusely, vomited twice, and

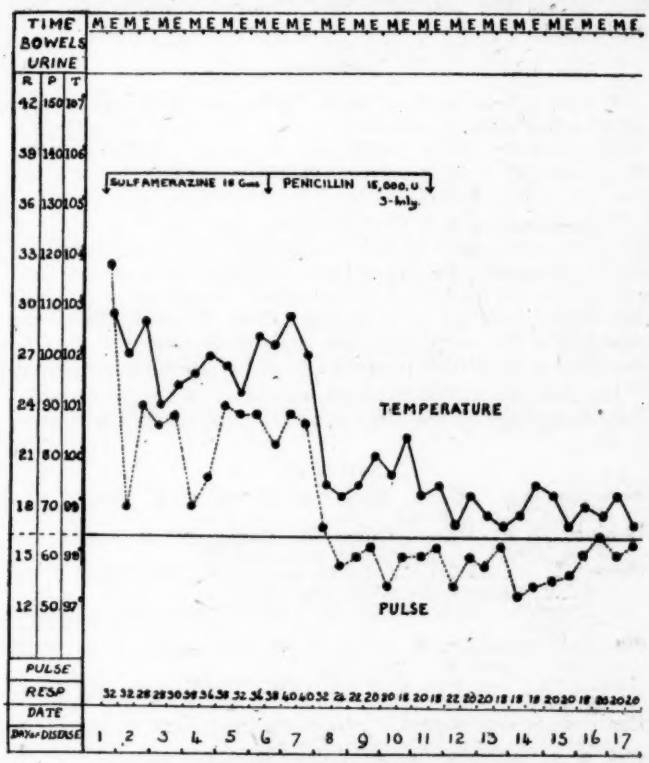

FIG. 2.—Chart of a typical case of staphylococcal pneumonia treated with sulphamerazine and penicillin.

felt weak. He had a cough with scanty sputum. Examination showed signs of left basal consolidation when he was admitted the following afternoon. Sulphamerazine was administered in the usual dosage, and produced a reduction in pyrexia to 100° F. (37.8° C.) from the original 103.6° F. (39.8° C.). On the 7th the pneumonic process had extended to the left upper zone, and herpes labialis was present. When on June 9 the bacteriologist reported that staphylococci were present in the sputum penicillin was started. In 30 hours the temperature had dropped to normal, and progress thereafter was uneventful. (The picture in this case was confused by an early finding of pneumococci in the sputum; had this not occurred the case would have been recognized as staphylococcal-resistant to sulphonamide sooner than on the fifth day of treatment.)

Toxic Effects

One patient showed on the third day a transient rubelliform rash which faded in spite of further administration of sulphamerazine. In this case, unlike those described

by Hall and Spink (1943), there was no relapse of temperature with the eruption.

Two women became confused during treatment. One has already been mentioned; she had had only 7 g. and her treatment was changed to penicillin. The other developed a psychotic state only after an adequate course of treatment had been given; the confusion cleared in four days and the pneumonia resolved rapidly. Drug psychosis has been reported by Flippin, Gefter, Domm, and Clark (1943), but both these cases had small doses of sulphonamide, and their condition may have been due to pneumonia rather than its treatment.

Drug fever occurs with all sulphonamides. Gefter *et al.* (1943) reported it in severe cases, most of which had over 40 g. of sulphamerazine. Two cases occurred in this series, the pneumonia responding according to expectation but fever persisting unexplained until a critical fall after stopping the drug incriminated the sulphonamide.

We have encountered no serious toxic manifestations in the use of this sulphonamide, and feel that they should be excessively rare provided that administration is not too prolonged.

Summary

A series of cases of primary pneumonia in adults is presented. No deaths occurred among 113 cases treated with sulphamerazine. Five deaths (7% mortality) occurred among 76 treated with other agents, including combined therapies. The total mortality was 3%.

It is claimed that sulphamerazine, which can be given in relatively small doses at eight-hourly intervals, is a satisfactory therapeutic agent for this disease. The results are such that pneumonia can be treated at home and be reduced to a "two-day fever." Should no response follow within 48 hours the case should be reviewed at once and the facilities provided by the hospital for further investigation and treatment be employed.

The need for radiological demonstration of complete resolution is emphasized, as is the need for adequate convalescence.

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Dr. Samuel Standard, the Associate Professor of Clinical Surgery at New York University, "has found that powder-puffs are a menace to health," reports B.U.P. "Anyone who has seen a powder-puff pulled out of a lady's handbag containing loose change, tobacco dust, and handkerchiefs, clean or otherwise, must have looked in awe as the perspired face and forehead were punished by swift, firm, hasty strokes smeared on fiercely by a deft, practised hand. Twenty-four hours later the owner of the face is surprised to find a crop of pimples spread over the cheek and forehead. In despair, she covers these again and again by the same method, and her wonder grows that her pimples multiply."

ORAL PENICILLIN IN TREATMENT OF PNEUMONIA IN THE ADULT

BY

T. ANDERSON, M.D.

AND

J. B. LANDSMAN, M.B.

(*From the University of Glasgow and Knightswood Hospital*)

A comparative study (Anderson and Ferguson, 1945) of the efficacy of the sulphonamides and penicillin in the treatment of pneumonia showed that there was little to choose between the two methods. Although certain advantages could be claimed for penicillin on account of its lack of toxicity, its use had one great drawback, especially for the general practitioner—the need for repeated intramuscular injections. Early studies with regard to the route of administration of penicillin had suggested that the material was likely to have little effect when given by mouth because of its inactivation by the acid of the gastric juice (Abraham *et al.*, 1941) or because of penicillinase production by coliform organisms (Chain and Florey, 1944). This led different workers to try to combine penicillin with suitable antacids and buffers designed to counteract the stomach acids (e.g., Little and Lumb, 1945). Bunn and his co-workers (1945) used penicillin orally in the treatment of 45 cases of pneumonia and had only one fatality. The material was given in a gelatin capsule; in about half of the cases the capsule contained an oily suspension and in the remainder the ordinary powdered sodium salt was enclosed. However, Finland, Meads, and Ory (1945) came to the conclusion that elaborate buffering devices were unnecessary and that administration with saline or even water was equally valuable in procuring effective therapeutic blood levels. These authors obtained satisfactory results with oral penicillin in the treatment of seven cases of adult pneumonia. Bushby and Harkness (1946), who reviewed the conflicting reports on different methods of administration, used penicillin orally for the treatment of gonorrhoea and were satisfied with the results, which indeed were as good as those obtained with intramuscular penicillin. (It is important to realize that these results were obtained in adults, for Buchanan (1946) has since shown that oral penicillin can be used with excellent effect in infants whose normal achlorhydria was assumed to prevent inactivation of the antibiotic.)

In view of the great variations in the sensitivity of different organisms to the action of penicillin and because of the differences in severity between cases of the same infection, it was felt that there was a need to investigate the efficacy of penicillin administered orally to an unselected series of patients with pneumonia. In this infection, unlike gonorrhoea, the treatment must be capable of dealing with the bacteria not only in the tissues but also in the blood stream; it seemed possible that penicillin given by mouth might be unable to attain concentrations in the blood high enough to quell a bacteriaemia.

Material and Methods

The patients comprised in the study were all adult males admitted to the wards of Knightswood Hospital during the winter of 1946–7 in whom the diagnosis of pneumonia was confirmed. They were divided into two groups, one group being given penicillin orally and the other penicillin intramuscularly as a control. There was no conscious selection of patients for either method; on admission they were allocated alternately to the two groups.

Intramuscular Penicillin.—The patients in this group were given an initial dose of 50,000 units, after which successive doses of 20,000 units were administered at four-hourly

intervals for a period of five days. Occasional severe cases received higher dosage in the early stages of treatment. The mean total dose of penicillin was 800,000 units.

Oral Penicillin.—Tablets of calcium penicillin with 0.5 g. of sodium citrate were used. They were made up to contain 20,000 and 25,000 units of penicillin, so that it was possible to vary the scheme of dosage. At first 40,000 units were given three-hourly, but it was soon apparent that this dose was too low, and thereafter for a considerable part of the trial the standard dose was 60,000 units three-hourly, at least during the early stage of treatment. Administration was continued for a period of five days. Towards the end of the trial further variations were made in the dosage, the principal one being that the three-hourly dose was reduced to 25,000 units after treatment had continued for 48 hours. The mean total dose given orally was 1,650,000 units. In order to avoid too much disturbance of the patient a double dose was given at midnight and the next dose at 6 a.m. Two measures were adopted in an endeavour to enhance absorption and to maintain effective blood levels: in the first place, the tablets were always administered along with a small amount (1–2 oz.: 28–56 ml.) of milk; and, secondly, the daily fluid intake was reduced to 2 pints (1.136 litres). Rather to our surprise this latter restriction was tolerated by the patients, and with adequate nursing supervision no difficulty was experienced in keeping the tongue moist and clean.

The bacteriological and clinical control was similar to that used in previous trials (Anderson and Ferguson, 1945). Pneumococcus typing from sputum was, however, somewhat restricted by the lack of adequate supplies of typing serum; the available supplies were kept for the examination of special cultures.

Results

The two groups of cases showed a fairly similar composition. The age distribution, duration of illness, and the presence of bacteriaemia are shown in Table I. It will be seen that in respect of the factors considered to have the greatest effect upon the prognosis there was little difference between the two groups. In so far as previous sulphonamide treatment was concerned routine estimations of the blood level on admission were not made during this trial. Of those who were given intramuscular penicillin 23 had received some sulphonamide before admission, but only seven had received more than 4 g. In the oral group the equivalent figures were 24 and 10, of whom two had received a single injection of penicillin intramuscularly.

TABLE I.—*Composition of the Two Treatment Groups*

	Intramuscular Penicillin	Oral Penicillin
Age distribution:		
0–20 years	0	3
21–40 ,,	14	13
41–60 ,,	22	18
61+ ,,	9	11
All ages	45	45
Bacteriaemia:		
Pneumococcus Type I	2	2
,, ,, II	5	7
,, ,, V	0	2
Others	2	2
Staphylococcus	0	1
Total	9	14
Duration of illness on admission:		
0–2 days	18	23
2–4 ,,	13	13
5+ ,,	14	9
Mean duration (days)	3·5	3·2

The effect of treatment in the two groups has been compared in respect of the duration of fever, the occurrence of complications, and the number and causes of deaths. The average *duration of fever* in uncomplicated cases was: "intramuscular" group, 1.9 days; "oral" group, 1.4 days. A composite temperature chart (Fig. 1) shows little difference between the effect of the two methods of treatment.

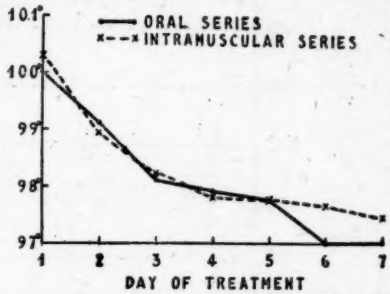

FIG. 1.—Duration of pyrexia in uncomplicated cases of pneumonia treated with penicillin.

Complications developed in 12 of the patients given intramuscular penicillin and in 16 of those given oral treatment. The individual complications are listed in Table II. It shows that there is no appreciable difference between the two groups.

TABLE II.—*Complications in the Two Treatment Groups*

Complication	Intramuscular Penicillin	Oral Penicillin
Lung abscess	2	0
Empyema	1	1
Sterile effusion	2	1
Delayed resolution	7	13
Lobar collapse	0	1

The patients who died are recorded in Table III, which includes relevant details regarding their clinical condition. Study of the table throws light on the present status of pneumonia therapy, for it is apparent that in many of the patients the presence of some accompanying disease or degeneration was a contributory factor which weighed too heavily against effective treatment. Thus in four of the patients other conditions were present which were of themselves sufficient to have produced a fatal issue. The mortality rate for the series is 7.8%, and when it is recalled that 20 of the patients were over the age of 60 years such a low rate may be regarded with satisfaction.

TABLE III.—*Deaths*

Case	Age	Method of Treatment	Duration of Illness Before Admission	Extent of Consolidation	Blood Culture	Complicating Factors	Cause of Death
D. B.	41	Oral	5 days	L1 + 2	Positive (I); pour-plate, 624 col./ml.	Chronic bronchitis; pulmonary tuberculosis	Pneumonia
J. C.	55	,,	6 ,,	R2 + 3	Positive (II); pour-plate, neg.	Severe anaemia; pulmonary tuberculosis (calcified)	—
J. G.	38	,,	2 ,,	L2 R3	Positive (II); pour-plate, uncountable	Chronic bronchitis. Died within 11 hours of admission	Early abscess formation at necropsy
M. W.	64	,,	,,	R1 + 2 + 3	Positive (V); pour-plate, neg.	Auricular fibrillation	No necropsy. Cardiac failure
D. M.	61	Intramuscular	5 ,,	L1 + 2	Positive (XVI); pour-plate, 20 col./ml.	Cirrhosis of liver	Pneumonia, resolved at necropsy
J. M.*	68	,,	4 ,,	L1 + 2	Sterile	—	Lung abscesses at necropsy
J. S.	58	,,	3 ,,	R1 + 2 L1	Positive (II); pour-plate, 11 col./ml.	Gross spinal deformity	Pneumococcal meningitis

L1 and L2 = Left upper and left lower lobe. The figure in parentheses under "Blood Culture" refers to the type of pneumococcus.
* Received sulphonamide treatment before admission.

Clinical details are given of two typical cases, one in the younger age group and the other, a particularly severe case, in the older age group.

Case 1

Treatment: penicillin orally—60,000 units three-hourly for 54 hours, then 40,000 units for 75 hours: total 2,120,000 units (Fig. 2).

A man aged 27 was admitted on Dec. 11, 1946; temperature 102° F. (38.9° C.), pulse 120, and respirations 40. On Dec. 8 he had had a sudden attack of shivering, followed by severe pain in the right chest anteriorly. Headache, troublesome cough, and rusty sputum were also noted. He had had several previous attacks of bronchitis. Sulphonamide had not been given before admission.

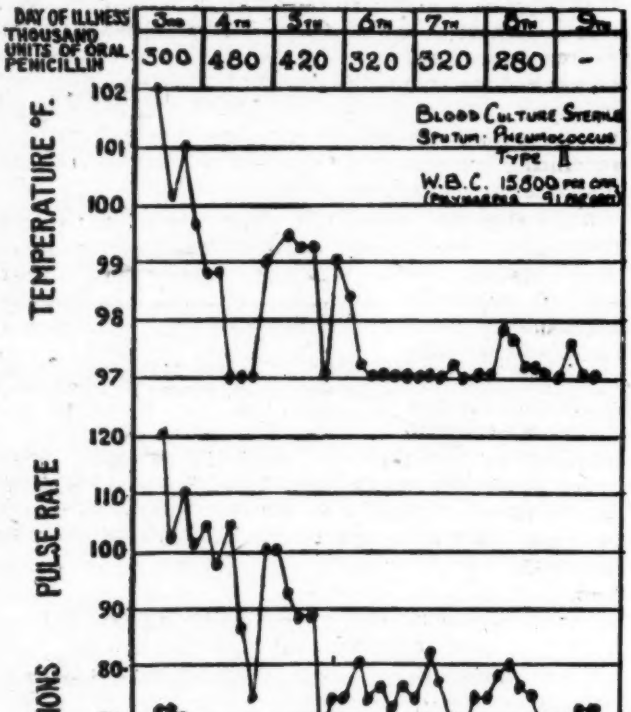
DAY OF ILLNESS
THOUSAND UNITS OF ORAL PENICILLIN
300 480 420 320 320 280 -
TEMPERATURE °F.
BLOOD CULTURE STERILE
SPUTUM: PNEUMOCOCCUS TYPE II
W.B.C. 13800 PER C.MM.
PULSE RATE
FL. OZS. RESPIRATIONS
INTAKE 30 40 40 40 40 40
OUTPUT 15 22 20 25 28 28

FIG. 2.—Chart of Case 1. Total penicillin, 2,120,000 units.

On admission the patient was acutely ill; his tongue was very dirty. Examination of the chest revealed a pneumonia involving the greater part of the right lung; this was later confirmed radiographically. Rales were numerous in both lungs, and there was a suggestion of spread of consolidation into the left lower lobe. The blood culture was sterile; sputum, pneumococcus Type II; W.B.C., 15,800 per c.mm. (polymorphs, 91%). Next day the temperature, pulse, and respirations fell and the patient's appearance improved, although there was no improvement in the chest signs. On the 15th, signs of consolidation were most pronounced in the middle third of the right lung. The general condition was much better. On the 23rd the chest was clear clinically and radiographically. The patient was discharged on Dec. 26.

Case 2

Treatment: penicillin orally—60,000 units three-hourly for 54 hours, then 40,000 units three-hourly for 57 hours: total, 1,840,000 units (Fig. 3).

The patient, a man aged 54, was admitted on Feb. 11, 1947, his sixth day of illness, having collapsed while at work. He complained of shivering, pain in the chest, cough, and sputum. He had had no previous illnesses, and no treatment had been given before admission. His temperature was 100° F. (37.8° C.), pulse 96, and respirations 28.

Physical examination showed a poorly nourished man who was acutely ill, cyanosed, and dyspnoeic. The tongue was dry and coated. There were signs of consolidation in both lower lobes. A blood culture performed on admission proved to be positive, and Type V pneumococci were so numerous on the pour-plate as to be uncountable. The W.B.C. numbered 6,400 per c.mm. (polymorphs, 93%). Next day the physical signs in both lungs were unchanged, and the cyanosis and dyspnoea were not improved. Auricular fibrillation was now present. Recovery was slow and uneventful, except for an elevation of

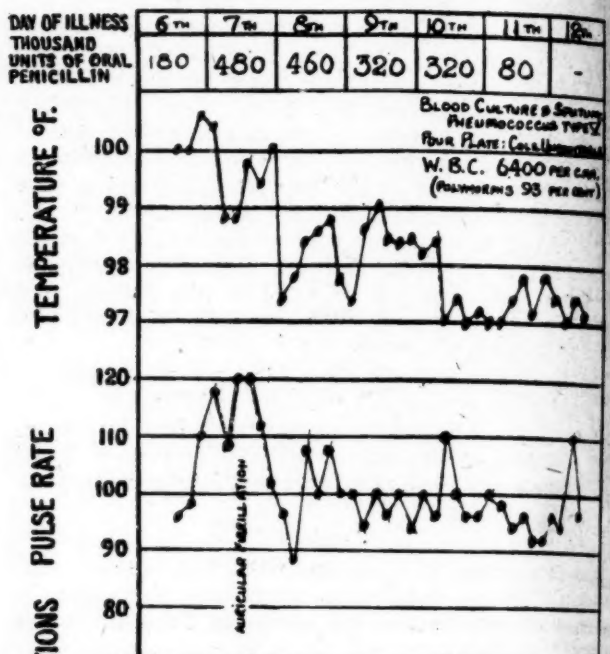
DAY OF ILLNESS
THOUSAND UNITS OF ORAL PENICILLIN
180 480 460 320 320 80 -
TEMPERATURE °F.
BLOOD CULTURE & SPUTUM: PNEUMOCOCCUS TYPE V
POUR PLATE: COLS. INNUMERABLE
W.B.C. 6400 PER C.MM. (POLYMORPHS 93 PER CENT.)
PULSE RATE
AURICULAR FIBRILLATION
FL. OZS. RESPIRATIONS
INTAKE 24 40 40 40 40 40
OUTPUT 30 31 44 35 38 36

FIG. 3.—Chart of Case 2. Total penicillin, 1,840,000 units.

temperature to 100.8° F. (38.2° C.) on March 1. At this time there was excessive prominence of old varicosities on the right leg, with surrounding redness. This subsided after 48 hours' rest in bed. When discharged after 36 days in hospital the chest had cleared except for a little basal rale.

Discussion

From the results recorded it is clear that the oral administration of penicillin is a satisfactory method of treatment for pneumonia. Our experience would suggest that treatment should start with a daily oral dosage equal to four times that required by the intramuscular route. After obvious clinical improvement (usually within 48–72 hours) this dose may be reduced by half. It is interesting that such a schedule is much smaller than that used by Bunn *et al.* (1945) and by Finland *et al.* (1945). When attention is directed solely to those patients who had bacteriaemia at the beginning of treatment it may be noted that in nine of them the colony counts were between 4 and 624 organisms per ml. and that in two others the organisms were too numerous to count. The satisfactory recovery of seven of these cases (including one of the latter) is good evidence of the efficacy of the oral method of

presentation. With regard to the technique of administration it would seem desirable at present to give the antibiotic as we gave it—namely, in milk and with a maximum fluid intake of 2 pints a day.

The necessity for a larger dose of penicillin makes it apparent that destruction of the antibiotic must take place at some part of its course through the body. Even with this increased dosage high inhibition levels in the blood serum were not obtained and indeed inhibition was rarely found in dilutions of serum above 1 in 2. Whether the state of the stomach juices during an acute infection such as pneumonia is an important factor in diminishing the amount of destruction may be worth further examination. One of us (J. B. L., unpublished) has shown that there is a decided diminution in the hydrochloric acid content of the gastric juice in pneumonia, and that this hypochlorhydric or achlorhydric state does not disappear immediately upon clinical recovery. The significance of such a finding is not at once apparent, but it may be a contributory factor in preventing an excessive destruction of penicillin. It would seem of some importance to make test-meal studies in other acute infections to see if this loss of hydrochloric acid is a common feature.

It should perhaps be emphasized that the indications for penicillin therapy are not changed by the present report. The sulphonamides constitute an adequate method of treatment for the majority of cases, more especially in the younger age groups; but for those patients who require penicillin there may be some advantage in the use of the oral route. In the first place, the difficulties associated with continued injections are overcome and treatment of pneumonia with penicillin in the home becomes practicable. Secondly, it seems possible that therapy might be cheapened by the use of substandard penicillin, which would not require the careful sterilization and packing necessary when used by injection.

The tablets were supplied by Burroughs Wellcome, to whom we are indebted for the opportunity of conducting the trial. We wish to thank Dr. F. Prescott and Dr. G. Brownlee for their advice and help.

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Man Against Pain: The Epic of Anaesthesia (By Howard Riley Raper. Victor Gollancz, Ltd. 1947. 10s. 6d.) can hardly be regarded as a serious contribution to the literature of the history of anaesthesia, for it is written for the lay public in a journalistic style. For example, in analgesia "the patient is woozie but not unconscious," and "avertin is administered per rectum in the form of a nice little pink enema." On the title page is the quotation: "If America had contributed nothing more to the stock of human happiness than anaesthetics, the world would owe her an everlasting debt of gratitude." The author develops this theme to such an extent that the British reader becomes rather irritated by his depreciation of much outstanding European work. For instance, the introduction of ether anaesthesia, together with an account of the controversy about Morton, Long, Wells, and Jackson, occupies 88 pages, while he dismisses Simpson's discovery of the anaesthetic properties of chloroform in just over one page. He ignores the pioneer work of British anaesthetists done during and after the 1914–18 war in evolving the inhalation technique of endotracheal anaesthesia and blind nasal intubation, yet fully describes the relatively trivial modification of using a cuffed tube instead of a gauze pack in a chapter entitled "The Dunked Dog."

ORAL PENICILLIN IN YOUNG CHILDREN

BY

A. I. SUCHETT-KAYE, M.D.Paris

AND

R. B. LATTER, M.B., Ch.B.(N.Z.), M.R.C.P.Lond.

(From St. Charles's Hospital, L.C.C.)

We report here a clinical trial in which we treated 25 children, originally diagnosed as suffering from pneumonia, with oral penicillin. It is hoped that our modest contribution will induce others to try out on a bigger scale the oral administration of penicillin in sick children. No references to systematic experiments in the treatment of pneumonia in young children with oral penicillin could be found in the literature, and therefore the instructions given, especially those regarding the dosage, had to be modified after experience had been gained from the first few cases.

The original instructions given were as follows: (*a*) Pharyngeal swabs to be taken before treatment, and the isolated organisms to be tested for penicillin sensitivity. (*b*) The chest to be *x*-rayed as soon as possible after admission and again at the completion of treatment. (*c*) A record of the fluid intake to be kept; no extra fluids to be given unless specially ordered. (*d*) Oral penicillin to be given 4-hourly (later modified to 3-hourly) except for the last night dose, which may be doubled if a prolonged uninterrupted sleep is desirable. Dosage: Infants up to 6 months, 10,000 units (later increased to 20,000 units); between 6 months and 1 year, 20,000 units (later increased to 30,000 units); over 1 year and under 2, 30,000 units (later increased to 40,000 units). The treatment was continued for five days or less according to progress made by the child. Each tablet contained calcium penicillin 20,000 i.u. and sodium citrate 0.5 g. One or more tablets were crushed in water or milk and given preferably before feeds.

The dosage was originally calculated according to body weight in the proportion of 50,000 units per 24 hours for a 14-lb. (6.3-kg.) baby—say 8,000 units 4-hourly day and night. This dosage was based on that of 500,000 units per 24 hours for a 10-stone (63-kg.) adult, an amount of oral penicillin apparently effective against pneumonia in the adult (Prescott, 1947, personal communication). Buchanan (1946) considered 4,000 units per lb. (0.45 kg.) of expected body weight per 24 hours effective in young children. In the more severe cases, especially the later ones, and in view of the results of serum-penicillin estimations, these doses and sometimes larger ones were given at 3-hourly instead of 4-hourly intervals. At most oral penicillin was given for five days, and in several cases where clinical improvement was rapid the treatment was discontinued earlier than the fifth day.

Clinical Results

Of the 25 children treated 2 were under 6 months old, 9 between 6 months and 1 year, and 14 between 1 and 2 years old. The revised clinical diagnosis in 18 cases was bronchopneumonia, in 5 lobar pneumonia, and in 1 bronchitis. The remaining child developed measles the day after admission; treatment was stopped and she was removed to a fever hospital. The five cases of lobar pneumonia and 11 cases of bronchopneumonia were considered seriously ill on admission. In 15 cases the diagnosis was confirmed by radiography. Most of the children had a history of one to three days' illness before admission, but 2 had been ill for as long as seven days. In most of the cases pneumococci and streptococci (principally

Str. viridans) were isolated from the upper respiratory tract; all these organisms proved to be penicillin-sensitive.

Four children failed to complete the course of treatment because they were sent on the third or fourth day to fever hospitals: one with acute meningitis and three with gastro-enteritis. All showed marked improvement of general and chest condition. They comprised the two children under 6 months and two in the group of those aged 1–2 years.

Four other children, who were gravely ill and failed to show any clinical improvement on oral penicillin after three or four days, were given sulphamezathine and recovered (see Table I). In two of these cases there is no record of what organisms were grown from the pharyngeal swabs; in one the predominant organisms were reported to be penicillin-sensitive, in the other penicillin-resistant.

TABLE I.—*Diagnosis and Treatment*

No. of Cases	Diagnosis	Oral Penicillin	Sulphonamides	Penicillin Course Not Completed
18	Bronchopneumonia	11	4	3
5	Lobar pneumonia	4		1
1	Bronchitis	1		

The 25th child developed measles the day after admission and is not included in the table.

The other children all had normal temperatures within 2–4 days and recovered uneventfully except for one infant, who has bronchiectasis and is still in hospital after three months. The average stay in hospital, apart from that spent by this child, those transferred to fever hospitals, and one taken home against advice on the tenth day, was 19 days, the shortest being seven days and the longest 35.

Serum-penicillin Levels

Estimations of serum-penicillin levels after oral administration of single doses of penicillin were made by the method described by Fleming and Smith (1947), who used a mixture of glucose, phenol red, and serum water as the culture medium and a streptococcus as test organism.

TABLE II.—*Serum-penicillin Levels*

Case No.	Age in Months	Dose in Units	Serum-penicillin Level (i.u./c.mm.) at Hours after Administration						
			½ hr.	1 hr.	1½ hr.	2 hr.	2½ hr.	3 hr.	4 hr.
1	7 months	20,000	0·25			0·06			—
2	3 ,,	10,000	0·03	0·25		0·03		—	
3	23 ,,	30,000		0·25		0·03			—
4	14 weeks	10,000		—		—		—	
5	12 months	20,000		—		—		—	
6	12 ,,	20,000	0·125		0·03		—		
7	22 ,,	20,000	0·06		0·03		—		
8	16 ,,	30,000	0·06		0·06		0·03		
9	15 ,,	30,000	0·03		0·06		0·125		
10	24 ,,	30,000	0·06		0·06		0·125		
11	11 ,,	20,000		0·125		0·03		—	
12	22 ,,	30,000		0·06		0·03		0·03	
13	20 ,,	30,000		0·06		0·03		0·03	
14	18 ,,	30,000		—		0·125		—	
15	7 ,,	30,000		1·0		0·5		0·25	
16	14 ,,	30,000		0·5		0·125		0·125	
17	23 ,,	40,000		1·0		0·25		0·125	
18	18 ,,	40,000		0·5		0·25		—	
19	9 ,,	20,000		—		0·03		0·125	
20	11 ,,	20,000		0·03		0·06		—	
21	8 ,,	20,000	0·125		0·06		0·06		

The mark — indicates no inhibition with standard streptococci.
The blood samples from Case 4 were stored for three days before testing and no penicillin could be detected. The blood samples from Case 5 were kept by mistake in the incubator for 24 hours and no penicillin could be detected.

Toxic Manifestations

Ellinger and Shattock (1946) reported a case of nicotinamide deficiency following administration of oral penicillin. They inferred that the nicotinamide deficiency was due to the effect of penicillin on the intestinal flora. Bushby and Harkness (1946), in a series of 85 adults, reported one case only of urticaria with oedema of hands, feet, and neck after oral penicillin.

Only one of our children developed, 10 days after completion of treatment, a blotchy urticarial rash. The temperature was slightly raised and diarrhoea was present. In another child, three days after treatment, a transient simple diarrhoea was noted. No pathogenic organisms were isolated from the stools of either case. Three other infants, transferred to fever hospitals, were diagnosed as having "gastro-enteritis"; their condition was excellent and the intestinal symptoms appeared on the third or fourth day during the course of oral penicillin. We think it possible that the diarrhoea in these cases was due to a direct toxic action of calcium penicillin on the digestive tract.

Comment

Oral penicillin appears to be effective against most varieties of acute pneumonia in childhood. Serum-penicillin estimations suggest that it should be. Some types of severe bronchopneumonia do not respond favourably, and for these parenteral penicillin and/or sulphonamides are the most efficacious. As György *et al.* (1946) rightly insist, for very sick children intramuscular penicillin is advisable, at least during the early acute phase of the disease. However, where circumstances are such that special nursing and frequent injections are impracticable, oral penicillin given in adequate doses at least 3-hourly will be of great benefit. If only for that alone the administration of oral penicillin is an important advance in chemotherapy.

Summary

Twenty-five young children were treated with oral penicillin. Of these 18 had bronchopneumonia, 5 lobar pneumonia, and 1 bronchitis; the remaining child was removed to a fever hospital with measles.

Of those with bronchopneumonia 11 made a satisfactory recovery on oral penicillin alone, 3 greatly improved but did not complete the course, and 4 failed to respond and were treated successfully with sulphonamides. Of those with lobar pneumonia 4 recovered on oral penicillin and 1, much improved, did not complete the treatment. One child with acute bronchitis recovered quickly in three days on oral penicillin.

In 21 children, all under the age of 2, serum-penicillin levels were estimated after a single oral dose varying from 10,000 to 40,000 i.u.; no penicillin was detected after three hours. The preparation used was calcium penicillin with sodium citrate.

Our thanks are due to Dr. E. A. Straker for performing the serum-penicillin estimations. We are indebted to Messrs. Burroughs Wellcome and Co. for supplying the tablets of oral penicillin.

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The Minister for Health has appointed a committee to examine the present system of medical education in Eire, and to recommend any necessary changes in the curriculum and in the arrangements for postgraduate education. The committee consists of: R. P. Farnan (chairman), Professors J. M. O'Connor, J. W. Bigger, W. J. O'Donovan, and S. Shea; F. Gill, president, Royal College of Surgeons in Ireland; B. Solomons, president, Royal College of Physicians of Ireland; J. C. Flood, Apothecaries' Hall of Ireland; A. A. McConnell, President, Royal Academy of Medicine in Ireland; A. Ryan, president, Medical Association of Eire; R. Atkinson Stoney, president, Medical Registration Council of Ireland; J. C. Saunders, Medical Superintendent Officer of Health, Cork; J. O'Hanrahan, County Surgeon, Roscommon; H. J. Moloney, S.C.; P. C. Cahill, M. Rynne, Legal Adviser, Department of External Affairs; T. O. Raifeartaigh, Chief Inspector of Secondary Schools, Department of Education; J. A. Deeny, Chief Medical Adviser, Department of Health; and J. Kearney, Inspector of Mental Hospitals, Department of Health. Dr. J. A. O'Sullivan, Medical Inspector, Department of Health, has been appointed secretary to the committee.

"LYMPHATIC REACTIONS" AMONG RELATIVES OF LEUKAEMIC PATIENTS

BY

S. N. ARDASHNIKOV

Department of Radiology, Molotov's Central Research Institute of Roentgenology and Radiology

In our first report (1934) we called attention to the extremely rare manifestation of the genotypical factors predisposing to leukaemia. This, taken together with a peculiar lymphatic reaction in a brother of a leukaemic patient, suggested the possibility of atypical cases, or "formes frustes," among the relatives of leukaemic patients. In fact, while leukaemia is not always manifest as such in bearers of the leukaemia genotypical factors, it might occasionally appear in some peculiar form of the disease. Some such cases of lymphatic reaction in members of a leukaemic family are described below.

Case Records

Case 1.—In this family in 1898 a 7-year-old girl died from leukaemia, although of what type could not be determined at this late date. The subject investigated is her brother, a 25-year-old engineer. On March 22, 1931, he felt generally unwell and weak and had a slight fever. A few days later he had a sore throat, and tonsillitis was diagnosed. This disappeared after a few days, but the pyrexia remained until April 6, rising in the evenings to 38–39° C. (100.4–102.2° F.) and falling in the mornings to 37.5° C. (99.6° F.). The patient continued to complain of general malaise and weakness. A blood analysis done on April 3 showed: Haemoglobin, 82%; erythrocytes, 4,980,000; leucocytes, 18,100 (rod-nuclears ("Stab"), 2%, polynuclears, 2%; eosinophils, 1%; lymphoidocytes, 92%; lymphocytes, 3%).

With a diagnosis of "lymphatic leukaemia" the patient was directed on April 17 to the Central Institute of Haematology and Blood Transfusion for treatment. A blood analysis made on April 19 at the Institute showed no leucocytosis, though it did reveal a considerable lymphocytosis and an increase in young forms: Haemoglobin, 70%; erythrocytes, 4,095,000; leucocytes, 7,500 (rod-nuclears, 7%; polynuclears, 10%; lymphocytes, 80%; monocytes, 3%). No abnormalities could be found except slightly enlarged submaxillary lymphatic glands and liver. On April 22 the patient left the Institute with a diagnosis of "lymphatic reaction following tonsillitis." Towards the end of 1932 the patient's blood was again examined because he complained of general weakness and some malaise; the analysis showed "absolute lymphocytosis." Our examination of the patient in 1933 showed no abnormality.

The patient's grandmother died of a liver complaint. His father and mother—first cousins—are living and show no blood anomalies. The same is true of the patient's brothers and sister.

The subject was under our constant observation. In May, 1937, he again had tonsillitis. Not being informed of this in time, we were able to take blood for analysis only on the third day after his recovery. The analysis showed the following: Leucocytes, 17,400 (rod-nuclears, 5%; polynuclears, 57%; eosinophils, 15%; lymphocytes, 34%; monocytes, 3%; Türck cells, 1%). The leucocyte count was thus increased, but there was only slight lymphocytosis.

This is a case, therefore, of a man who is a member of a leukaemic family and who shows a peculiar lymphatic reaction expressing itself as an absolute lymphocytosis and leucocytosis during an infection of the throat a month after the symptoms of tonsillitis have disappeared, and even independently of any infection.

Case 2.—This case concerns a pair of identical girl twins. Twin A, 11 years old, entered the clinic on Sept. 29, 1936, with a diagnosis of acute rheumatic polyarthritis and diseased mitral valve.

The patient had pneumonia when 2 months old, German measles at 18 months, chicken-pox at 5 years, and at 6 years tonsillitis (possibly diphtheria) complicated by paralysis of the limbs and pains in the joints, the condition lasting about three months. Up to 6 years of age she often had attacks of false croup and "chills." When 8 years old she had paratyphoid fever, and at 12 measles. From early childhood up to 8 years of age she suffered from broncho-adenitis.

The following information was obtained from the patient herself and her mother, and was confirmed by reference to case records and the statements of her physician. On March 28, 1935, the patient suddenly became feverish, her temperature rising to 39.8° C. (103.6° F.). The temperature then rose at noon, in the evening, and sometimes in the morning. The liver and spleen were enlarged to almost double normal size. The cervical, axillary, and inguinal lymphatic glands were greatly enlarged. Blood examined for malaria parasites was negative. Blood analysis (April 7): Haemoglobin, 70%; erythrocytes, 4,100,000; leucocytes, 24,000 (rod-nuclears, 3%; polynuclears, 2%; lymphocytes, 93%; monocytes, 1%; Türck cells, 1%); polychromasia was seen. The analysis thus revealed that the patient had considerable leucocytosis and marked lymphocytosis. A later analysis confirmed these findings.

After a week's time the patient's temperature fell to 37.3° C. (99.2° F.), but on April 10 symptoms of tonsillitis appeared—complaint of sore throat, small patches of membrane, reddened pharynx—and bacteriological examination revealed the presence of streptococci. Two or three days later the temperature returned to normal. Liver, spleen, and glands decreased in size. Blood analysis made on April 18 showed decreased leucocytosis but still considerable lymphocytosis: Haemoglobin, 72%; erythrocytes, 3,980,000; leucocytes, 7,000 (polynuclears, 28%; eosinophils, 1%; lymphocytes, 65%; monocytes, 6%).

In view of the still abnormal blood picture the patient was directed to the children's clinic of the First Moscow Medical Institute to have the diagnosis checked. According to the case-history records all lymphatic glands were enlarged, the spleen was palpable at the costal margin, and the liver was enlarged 2.5 cm. Though numerous blood analyses were made, the number of leucocytes were never found to be above 6,000–7,000. Lymphocytes remained constantly at 70–80%. In July, 1935, the patient left the clinic with the diagnosis of "lymphatic reaction following tonsillitis." Shortly afterwards petechiae appeared on the patient's body and disappeared after a few days. There was no rise of temperature and no enlargement of the glands. The patient was under observation for a year by the Central Institute of Haematology and Blood Transfusion. Data from the subject's blood analyses after she left the clinic of the First Moscow Medical Institute, obtained between June 26, 1935, and April 13, 1936, are presented in Table I.

TABLE I

Date of Analysis	Hb %	Erythrocytes	Leucocytes	Rod-nuclears	Polynuclears	Eosinophils	Basophils	Lymphocytes	Monocytes
April 26, 1935 ..	64	3,880,000	4,800	3	40	5	—	46	6
July 13, 1935 ..	70	4,320,000	6,000	—	43	2	—	52	3
Sept. 8, 1935 ..	70	3,650,000	4,800	—	52	4	—	38	6
Sept. 23, 1935 ..	63	4,010,000	7,400	0·5	31·5	2	—	60·5	5·5
Oct. 24, 1935 ..	63	4,010,000	6,700	—	—	—	—	60	—
Nov. 29, 1935 ..	64	4,200,000	4,600	0·5	56·5	3	—	36	4
Dec. 25, 1935 ..	58	3,600,000	6,800	0·5	27	1·5	0·5	68	2·5
April 13, 1936 ..	50	4,420,000	4,400	0·5	19	5	—	70·5	5

As the table shows, while the leucocyte count is normal or only slightly increased, there is a definite tendency towards increase in the lymphocyte count, and this despite the long period of time elapsed (over a year) since the increase started.

From July 4 to 8, 1936, the patient was ill with colitis (? dysentery). The temperature rose to 39.6° C. (103.3° F.). After the colitis the patient complained of pain in both knee-joints; there was no swelling or redness, and the temperature remained normal. The pains went within four days. A month later symptoms of colitis recurred. Temperature rose to

37.8° C. (100° F.). After a week the colitis and pyrexia disappeared. On the morning of Sept. 11 the patient vomited, became somnolent, but was not feverish. A blood analysis made at this time showed : Haemoglobin, 60% ; erythrocytes, 3,800,000 ; leucocytes, 10,000 (rod-nuclears, 3% ; polynuclears, 55% ; eosinophils, 2% ; lymphocytes, 30% ; monocytes, 10%); sedimentation rate, 30 mm. per hour.

On Sept. 12 the right knee-joint became swollen and painful, the temperature remaining normal. The next day the same condition occurred in the left knee-joint. Several days later both ankles became slightly swollen, and the temperature rose in the evenings to 38.2° C. (100.8° F.). During one of the attacks of pain in the joints the patient's body began to jerk all over ; the convulsive movements ceased when bromides were given. In this condition the patient entered the clinic. Clinical examination confirmed findings typical for rheumatic polyarthritis and endomyocarditis. The glands were slightly enlarged in the cervical and axillary regions ; liver and spleen were normal. In view of the somewhat peculiar reaction of the patient's blood-forming organs to infection, noted in the history, we record in Table II the data from blood analyses made during her stay in the clinic.

TABLE II

Date of Analysis	Hb %	Erythrocytes	Leucocytes	Rod-nuclears	Polynuclears	Eosinophils	Lymphocytes	Monocytes
Sept. 29, 1936 ..	71	4,230,000	8,400	1	39	7	25	8
Oct. 10, 1936 ..	58	3,780,000	5,300	3	28	2	64	2
Oct. 14, 1936 ..	—	—	10,000	2	43	—	53	2
Oct. 22, 1936 ..	60	3,760,000	6,700	—	41	3	51	5
Nov. 3, 1936 ..	69	4,120,000	6,100	2	56	3	33	6

The recurrence of lymphocytosis (Oct. 10, 14, and 22) is noteworthy in a case of acute polyarthritis, where one ordinarily expects a slightly increased number of neutrophils together with fewer lymphocytes and eosinophils. The subject's lymphatic system produced a different blood picture from that usually described in rheumatic infection. In this case the blood analyses in Table III, *made after the patient's recovery* and release from the hospital, show the recurrence of lymphocytosis.

TABLE III

Date of Analysis	Hb %	Erythrocytes	Leucocytes	Rod-nuclears	Polynuclears	Eosinophils	Lymphocytes	Monocytes
Nov. 13, 1936 ..	60	3,800,000	10,000	3	55	2	30	10
Nov. 25, 1936 ..	68	4,500,000	6,800	2	41	5	46	6
April 16, 1937 ..	67	4,200,000	6,000	2	45	2	47	4

The patient's lymphatic system reacted with considerable lymphocytosis to both tonsillitis and rheumatism. The occurrence of identical reactions to both these infections is all the more remarkable, because, while in some cases tonsillitis is accompanied by lymphocytosis (although not so marked, it is true, as in our patient), polyarthritis as was revealed here is usually accompanied by relative lymphocytopenia. The data given acquire special interest in view of the fact that, suspecting a connexion between " lymphatic reaction " and leukaemia in the family, as occurred in the first case discussed here, we investigated and found that this patient actually does come from a family affected with leukaemia. Her maternal grandfather, 70 years old, fell ill with leukaemia on June 3, 1935. His blood analysis, done on June 21, showed : Haemoglobin, 51% ; erythrocytes, 3,990,000 ; leucocytes, 177,000 (polynuclears, 7.5% ; lymphocytes, 90.5% ; monocytes, 2%).

Clinical examination at this time disclosed considerable enlargement of all lymphatic glands, especially the submaxillary and right axillary. The liver was palpable at the costal margin and the spleen was enlarged. Keeping in mind the instability of the lymphatic system in the grand-daughter, we had the grandfather taken to hospital on Oct. 19, 1936, and placed under our observation. His condition, with the enlarged lymphatic glands and spleen in conjunction with the blood picture, left no doubt about the nature of his disease—a typical case of chronic lymphatic leukaemia. Further investigation disclosed that his elder brother had died in 1909 at the age of 48 of a similar disease.

As our assumption that some connexion exists between leukaemia and specific blood reactions in the members of the same family was thus confirmed to a certain extent, we naturally sought the reasons for such a connexion in the data available on the other twin, who had died four years previously of tuberculous meningitis.

Twin M had the same diseases in childhood as her sister. On March 5, 1931, M became ill with exudative pleuritis, and on April 22 she entered the clinic at the Medico-Genetical Institute with a diagnosis of " exudative pleurisy (tuberculous), broncho-adenitis." A blood analysis made then showed only slight leucocytosis but marked relative lymphocytosis: Haemoglobin, 60% ; erythrocytes, 4,450,000 ; young granulocytes, 0.5% ; rod-nuclears, 4.5% ; polynuclears, 36.5% ; eosinophils, 0.5% ; lymphocytes, 64.5% ; monocytes, 2.5% ; Türck cells (?), 1%. Although lymphocytosis does occur in pleuritis of the tuberculous type, the proportion of lymphocytes (64.5%) revealed by the analysis is certainly somewhat unusual.

The patient was kept under observation at a tuberculosis dispensary for a month and a half after her discharge from the clinic. She died of " tuberculous meningitis " late in July, 1931, at Botkin Hospital. At the necropsy tuberculous infiltration of the left subclavicular region and tuberculous leptomeningitis of the base of the brain were found. During this last illness one blood analysis was made, which, however, disclosed no lymphocytosis.

Thus in the family investigated the first twin revealed a peculiar anomaly of the lymphatic system which showed in its reaction to infection. There was considerable leuco- and lymphocytosis, the latter rising to 90% and higher. Although we cannot be equally positive in our statements about the second twin, there was undoubtedly a certain peculiarity in the lymphatic reaction to infection. In view of the great rarity of leukaemia itself and the equal or even still greater rarity of reactions such as those here described, the occurrence of both phenomena in members of one and the same family can hardly be regarded as a coincidence. Of particular significance is the second case, where previously made assumptions of leukaemia in the family and lymphocytosis in the second twin were confirmed on investigation. If, as in this case, we note a certain relationship between lymphatic leukaemia and lymphatic reactions in the relatives, the question now arises of the nature of these lymphatic reactions. Are they early or concealed forms ? What is their pathogenesis, prognosis, etc. ? The material presented in this paper is of course insufficient to warrant an answer to these questions. However, our third case does offer a few indications toward the solution.

Case 3.—This case is one of the familial cases described in our first communication. Patient R became ill with chronic lymphatic leukaemia, according to her statement, in October, 1932. A blood analysis made in 1927 showed : Haemoglobin, 60% ; erythrocytes, 3,350,000 ; slight lymphocytosis (?) ; eosinophils, 11%. Roundworms were found in the faeces. An analysis taken in 1928 gave the following data : Haemoglobin, 60% ; erythrocytes, 5,140,000 ; leucocytes, 9,000 (eosinophils, 2% ; lymphocytes, 55.5%). At that time the patient paid no attention to the lymphocytosis. Towards the end of 1932 she accidentally noticed a swelling of the lymphatic glands in the left axillary region and, later on, in other regions. A blood analysis then showed : Haemoglobin, 65% ; erythrocytes, 3,580,000 ; leucocytes, 150,000 (lymphocytes, 96%).

This marked lymphocytosis dispelled all doubts about the presence of lymphatic leukaemia. Thus we see again a member of a leukaemic family who at one time showed a lymphatic reaction. This case is interesting not so much on account of the lymphatic reaction itself but because we now find the patient presenting a clear picture of chronic lymphatic leukaemia. So far this case is the only one we know of its kind, and no

conclusions can yet be drawn from it. Nevertheless, it does indicate certain possibilities for further investigation into the pathogenesis of leukaemia.

Discussion

The first two cases present pictures of an atypical course of infection characterized by marked lymphatic reaction. Observations on leukaemoid and lymphatic reactions in infection are not new, and in fact have even served as arguments in favour of the infectious origin of leukaemia. However, what is new in our cases is the fact that all the patients come from families affected with leukaemia. While in the first case we accidentally discovered a leukaemic patient in the subject's family, and in the third case investigated the subject only in the stage of definitely developed lymphatic leukaemia, knowing beforehand that we were dealing with a familial case of leukaemia, the second case differs in that we based upon the existence of a lymphatic reaction in one of the twins the assumption that leukaemia existed in the family and then on investigation found this to be correct. Furthermore, our discovery of leukaemia in this last case led us to assume the presence of a lymphatic reaction in the second twin. To a certain extent this assumption was also confirmed.

It seems to us that chance does not explain the occurrence of a lymphatic reaction in all these cases. In our first communication we had already stated that in lymphatic leukaemia heredity apparently played some role. If we assume the possibility of a poor manifestation of the leukaemia genotype, most probably it would take precisely the form of lymphatic reaction. Naturally it does not follow from this that all individuals exhibiting a lymphatic reaction in some disease must belong to families affected with leukaemia, and on the other hand not all bearers of leukaemia genes exhibit such a reaction. However, there can be no question but that cases where such a relationship is established cannot be ignored, for they contribute to the explanation of such reactions.

Special consideration must be given to the phenomenon met with in our second case, where the abnormal blood picture remained for a long time. The question may be put as follows: Are we really dealing here with a stable deviation in the blood composition occurring after streptococcal tonsillitis, or is this somewhat variable lymphocytosis simply the peculiar constant state of our subject's lymphatic system? This question can be answered correctly only by comparing the data from blood analyses made before and after the onset of the disease. We give below the data from two of twin A's blood analyses taken from the records of the Medico-Genetical Institute. The first of the two was made in March, 1931, when twin A entered the institute's clinic for the treatment of tuberculous intoxication and broncho-adenitis. The twins were at the time aged 8 years 10 months. Blood analysis: Haemoglobin, 64%; erythrocytes, 3,500,000; leucocytes, 8,200 (rod-nuclears, 1%; polynuclears, 17%; eosinophils, 3.5%; lymphocytes, 72%; monocytes, 4%). The second analysis, dated Dec. 7, 1932, gave the following data: Haemoglobin, 53%; erythrocytes, 4,160,000; leucocytes, 7,300 (rod-nuclears, 2%; polynuclears, 28%; eosinophils, 1%; lymphocytes, 59%; monocytes, 10%). The considerable lymphocytosis revealed in both analyses is unusual for tuberculous intoxication but can be fully explained in this case, as in her tonsillitis, by the instability of the subject's lymphatic system, which reacts with a lymphocytosis to any infection regardless of its origin. At the same time there is another possibility that should not be overlooked—namely, that the lymphocytosis is due to a combination of two processes: (1) a peculiar condition or "set-up" of the lymphatic system in which a 40–60% leucocyte count is to be considered "normal," and (2) the influence of infection.

The material discussed above, pointing to the possibility that the leukaemia genotype may manifest itself in a peculiar manner—in the cases here described, in lymphatic reaction—takes on special significance in view of the data acquired in recent years by medical genetics in the field of early and latent forms of hereditary diseases. Most pathological genes in man are characterized by poor, sometimes surprisingly low, penetrance. Without going into the theoretical aspect of the problem of penetrance, we believe it useful to emphasize here certain points bearing on the facts discussed in this paper. In a number of researches into such diseases as hypertension (Ryvkin and others), ulcer and cancer of the stomach (Levin and Kuchur), pernicious anaemia (Presnyakov), diabetes insipidus (Pesikova), and other diseases where both the patients and their relatives were clinically examined, the existence of such latent manifestation was confirmed. The patient's relatives showed one or another symptom characteristic for the patient's disease. For example, one may mention the finding of achylia among the relatives of patients with cancer, some disturbance of blood flow and blood pressure among relatives of subjects of hypertension, the achlorhydria in relatives of people with pernicious anaemia, etc. Our material on the expression of the leukaemia gene in man does not present an isolated phenomenon in the hereditary pathology of man.

Mention should be made in this connexion of J. Bauer's opinion that lymphocytic, monocytic, and myeloid reactions are abortive forms of leukaemia. We consider this to be a very interesting but scarcely proved hypothesis. Our investigation throws some light on the nature of these reactions. In future the essential task in studying each individual case of lymphatic reaction will be to complement the usual clinical examination with a thorough family history and investigation of the patient's close relatives.

Summary

This investigation is devoted to a study of concealed forms of leukaemia. The surprisingly rare manifestation of the leukaemia genotype, combined with the discovery of a peculiar lymphatic reaction in the brother of a leukaemic patient (Case 1), led us to search among the members of families affected with leukaemia for such relatives who might exhibit some symptoms of the disease.

We describe three cases of a peculiar lability on the part of the lymphatic system in several relatives of leukaemic patients. The peculiarity is expressed in a lymphatic reaction, associated in particular with infection.

Besides finding subjects with this lymphatic reaction among the relatives of leukaemic patients (Cases 1 and 3), we worked in the opposite direction and found people with a high leuco- and lymphocyte count in families from which leukaemic patients came (Case 2). Noting a peculiar lymphatic reaction in one twin, we assumed the presence of leukaemic patients in the family; this supposition was confirmed on investigation. A supposition that the second twin must have shown a lymphatic reaction while suffering from some infectious disease was to a certain extent also confirmed.

It would seem that the association between leukaemia and lymphatic reactions is not accidental and must be due to the influence of the leukaemia genotype.

Some indication of the prognosis in cases with these lymphatic reactions can be gained from the third case, where a leukaemic patient had shown a lymphatic reaction four years before falling ill.

This investigation is only a first step in the study of the expression of the leukaemia gene.

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PRODUCTION OF Rh AGGLUTININS ANTI-C AND ANTI-E BY ARTIFICIAL IMMUNIZATION OF VOLUNTEER DONORS

BY

J. J. VAN LOGHEM, M.D.

With the Technical Assistance of Miss M. v. d. HART

(From the Centraal Laboratorium van den Bloedtransfusiendienst, Binnengasthuis, Amsterdam)

The Rh agglutinins anti-C and anti-E used for Rh subgroup typing have until now been obtained from mothers and patients with agglutinins induced by Rh antagonism. It is possible to increase the titre of these antibodies by artificial immunization with the specific antigens C or E (R′ or R″ cells). If these sera are obtained from Rh-negative persons they usually contain incomplete anti-D antibodies as well.

In order to obtain pure anti-C and anti-E agglutinins without incomplete anti-D the following experiments were performed in the Central Laboratory of the Blood Transfusion Service in Amsterdam.

Rh-negative male volunteer donors were injected with R′r (Cde/cde) and with R″r (cdE/cde) cells. This procedure is very simple.

F. K., a male volunteer donor aged 18, blood group O rr, was treated in the following way.

He received five injections of 2 ml. of R″r cells of group O, followed by seven injections of 0.25 ml. (injections twice a week). After a period of rest for nearly six weeks five further injections of 0.25 ml. of blood were given with approximately the same time intervals. During this period no Rh agglutinins were present in his serum. After the last injection of 0.25 ml. of R″r blood (17th injection from the beginning) a chill with rise of temperature resulted. Rh agglutinins type anti-E with titre 1:16 could now be demonstrated (the titre in saline was the same as in albumin). After a new series of nine injections during 27 weeks the titre increased to 1:32 in saline and to 1:128 in albumin (see Table I).

TABLE I.—*Donor F. K. (Blood Group O rr)*

Date	No. of Inj.	Quantity of R″ Cells given I.V. (ml.)	Rh Antibodies				
			Early-immune		Hyperimmune		
			E	D	E	D	
11/11/46 ..	1	2·0					
18/11/46 ..	2	2·0					
25/11/46 ..	3	2·0					
2/12/46 ..	4	2·0					
5/12/46 ..	5	2·0					
9/12/46 ..	6	0·25					
12/12/46 ..	7	0·25					
17/12/46 ..	8	0·25					
20/12/46 ..	9	0·25					
24/12/46 ..	10	0·25					
30/12/46 ..	11	0·25					
6/1/47 ..	12	0·25					
13/2/47 ..	13	0·25					
17/2/47 ..	14	0·25					
20/2/47 ..	15	0·25					
3/3/47 ..	16	0·25					
7/3/47 ..	17	0·25					
8/3/47 ..			1:16*	—	1:16	—	Chill and rise of temp.
10/3/47 ..	18	0·10	1:64†	—	?	—	
17/4/47 ..	19	0·10					
24/4/47 ..	20	0·05					
28/4/47 ..	21	1·0	1:64†	—	?	—	
5/6/47 ..	22	1·0					
13/6/47 ..	23	0·5					
21/7/47 ..	24	0·5					
8/9/47 ..	25	1·0					
18/9/47 ..	26	0·5	1:32		1:64 1:128†		

* Visible macroscopically. † Weakly positive macroscopically.

In this way it is proved that it is possible to produce a pure anti-E antibody by repeated injections with R″ cells. Besides the complete anti-E (early-immune) antibodies, it seems that incomplete (hyperimmune) antibodies type anti-E were also formed.

Encouraged by this success five other male volunteer donors were injected with R′ cells, group O (donor Sch. R′R′ and donor Dam. R′r). Practically the same procedure of immunization as in the first case was followed. Only one of these donors seemed to be sensitive enough to produce Rh antibodies.

G. de J., a male volunteer donor aged 33, blood group A rr (see Table II). After the 13th injection Rh agglutinins were present in his serum (titre 1:2). After the 17th injection with R′ cells of group O the titre increased to 1:8 (visible macroscopically), 1:16 weakly positive, type anti-C, with incomplete antibodies type anti-D, titre 1:8 (albumin test) without incomplete (or hyperimmune) anti-C. After a new series of 11 injections the titre of anti-C in saline fell to 1:4, but increased in albumin to 1:16. After four more injections the titre in saline was unchanged, but in albumin it increased to 1:32.

TABLE II.—*Donor G. de J. (Blood Group O rr)*

Date	No. of Inj.	Quantity of R′ Cells given I.V. (ml.)	Rh Antibodies				Cell Suspension R′
			Early-immune		Hyperimmune		
			C	D	C	D	
11/3/47 ..	1	2·0					Sch.
14/3/47 ..	2	1·0					"
17/3/47 ..	3	1·0					"
20/3/47 ..	4	0·25					"
24/3/47 ..	5	0·25					"
27/3/47 ..	6	0·25					"
3/4/47 ..	7	0·25					"
8/4/47 ..	8	0·25					"
10/4/47 ..	9	0·25					"
19/5/47 ..	10	0·25					"
27/5/47 ..	11	0·25					"
2/6/47 ..	12	0·25					Dam
5/6/47 ..	13	0·25					Sch.
			1:2				
9/6/47 ..	14	0·25					Dam
12/6/47 ..	15	0·25					Sch.
16/6/47 ..	16	0·25					Dam
19/6/47 ..	17	0·25					Sch.
			1:8*		—	1:8	
23/6/47 ..	18	0·25					Dam
3/7/47 ..	19	0·25					Sch.
10/7/47 ..	20	0·25					"
21/7/47 ..	21	0·25					Dam
24/7/47 ..	22	0·25					Sch.
28/7/47 ..	23	0·25					Dam
3/8/47 ..	24	0·25					Sch.
14/8/47 ..	25	0·25					Dam
21/8/47 ..	26	0·25					"
25/8/47 ..	27	0·25					"
29/8/47 ..	28	0·25					"
			1:4		1:16		
4/9/47 ..	29	0·25					"
11/9/47 ..	30	0·25					"
19/9/47 ..	31	0·25					"
22/9/47 ..	32	0·25					"
			1:4		1:32	1:8	

* Visible macroscopically.

Thus it appears to be necessary to stop the immunization at the right moment in order to prevent the production of the hyperimmune antibodies, which sometimes cause a decrease in titre of the early-immune antibodies.

In cases of erythroblastosis foetalis Diamond demonstrated that after repeated immunizations Rh agglutinins (early-immune antibodies) are replaced by (or changed into) Rh-hyperimmune antibodies. In these two cases of artificial immunization these findings could be confirmed.

Four other donors treated in the same way have failed to produce Rh antibodies.

So long as there are found anti-D antibodies of the incomplete type only artificial immunization of male volunteer donors is a useful method in preparing anti-C and anti-E agglutinins.

Note on the blood of the two donors to G. de J.; by R. R. Race, M.R.C.S., L.R.C.P. (Medical Research Council, Blood Group Research Unit, Lister Institute, London)

The finding of some anti-D as well as the hoped-for anti-C in the serum of volunteer G. de J. was of considerable theoretical interest, for it appeared that the antigen C might be capable of stimulating the antibody anti-D. It therefore became important to test the cells of the two R′ donors as fully as possible in order to detect the antigen D^u if it should be present. Agglutination tests gave the following results:

	Anti-						
	C	C^w	c	D	E	e	
Donor Dam. ..	+	−	+	−	−	+	i.e., apparently Cde/cde (R′r)
Donor Sch. ..	+	−	−	−	−	+	Cde/Cde (R′R′)

When these two bloods were further tested with many anti-D sera (using the saline, albumin, and antiglobulin techniques) some of the reactions were positive; that is to say, the samples should more properly be called CD^ue/cde and CD^ue/Cde. There are several grades of the D^u antigen distinguishable by the different proportion of anti-D sera with which they react. The D^u antigen in these two bloods was low on the scale.

In view of the close relationship between the antigen D and the antigen D^u, it seems reasonable to attribute the anti-D antibody in the serum of the volunteer to the D^u antigen present in the blood of both his donors.

Medical Memoranda

Two Cases of Fugue after Mepacrine Administration

Although it is by no means certain that the administration of mepacrine ("atebrin") was the cause of the fugues here described it is felt that these case notes should be placed on record because of the striking sequel in both cases to moderately heavy doses of the drug and because of the tragic circumstances which ensued in Case 1. Both cases occurred in the Anglo-Egyptian Sudan.

CASE REPORTS

Case 1.—The patient, a happily married British woman aged 32, with two children, had no family or personal history of mental disorder and no private worries. She was first seen on Oct. 16, 1945, by a Sudanese doctor in an out-station. She was suffering from fever (temperature 103° F.=39.4° C.) and severe headache. M.T. malaria was diagnosed by blood examination, and the following course of mepacrine was given: First day, 0.3 g. followed by 0.3 g. three hours later; second to fourth days (inclusive), 0.2 g. night and morning—total, 1.8 g. The condition responded quickly to treatment, and on Oct. 19 the patient felt fit and well. She asked permission to play tennis, but this was refused. That night, after dinner, she and her husband retired to bed at about 9.30 o'clock. They chatted for a while in bed and the patient appeared to be her normal cheerful self. The following morning the husband awoke to find that his wife had disappeared. Shortly afterwards some natives arrived with the news that her body had been found in the river. Post-mortem examination showed that death had been due to drowning, and there were no other abnormal findings.

Case 2.—A British man aged 47, with no family history of mental disorder, had suffered from claustrophobia after the 1914–18 war due to having been buried alive three times by shell bursts, but the condition had completely cleared up by 1924. I saw him on Nov. 3, 1945, when he was suffering from fever (temperature 101° F.=38.3° C.) and pains in the back and bones. M.T. malaria was diagnosed by blood examination and he was put on the following course of treatment: First day, 0.2 g. of mepacrine followed by 0.2 g. after four hours; second to fifth days (inclusive), 0.1 g. of mepacrine t.d.s.; sixth to tenth days (inclusive), 10 gr. (0.65 g.) of quinine bihydrochloride t.d.s. On the evening of the sixth day of treatment the patient felt sick after taking quinine. On the seventh day, without medical advice, he decided to revert to mepacrine treatment and proceeded to take 0.1 g. t.d.s. On the evening of the ninth day—i.e., after he had taken a total of 2.4 g. of mepacrine, he went to his bath at his usual hour of 6 p.m. While sitting in the bath he felt a "feeling of unreality coming over him." The next thing he knew was that he was sitting in his dining-room naked and wet. The interval of amnesia had lasted for about half an hour. Mepacrine was at once stopped and no further ill effects occurred.

I have to acknowledge with thanks the permission of the Director, Sudan Medical Service, to publish these notes.

D. R. MACDONALD, M.B., Ch.B., M.R.C.P.,
Sudan Medical Service.

Unusual Case of Calcification of the Myocardium

Calcification of the heart to a great extent, without a previous history of pericarditis or other heart disease, is rare, and the facts revealed by the following case report are, I believe, unusual.

CASE HISTORY

The patient was admitted to hospital when 35 years of age, suffering from dementia and mental deficiency. It was stated by his relatives that he had not had any previous illnesses. His clinical record during the whole of his fifteen years in hospital showed that at all times he suffered from slight dyspnoea and cyanosis of both hands and feet, and occasionally he had swelling of the lower extremities. Attendants who were in close contact with the patient during the whole of his hospital life state that although he never actually worked he was quite capable of walking about and attending to his own needs. During the last four years he was confined to his bed, but got up every day for toilet purposes. One morning, fifteen years after admission, just after he had returned to bed he suddenly collapsed and died. He was then 49 years of age.

At necropsy the main pathological changes were found in his heart. This organ was enlarged (weight 360 g.) and felt extremely hard, in fact the usual post-mortem scissors would not cut into its substance, and bone forceps had to be used. The pericardium was fused completely over the whole surface of the left ventricle. The latter on being opened was found to contain ante-mortem clot (see illustration). In the lower two-thirds of the left ventricle there was no muscle tissue left at all; it was simply an ossified wall, which was obviously the result of a fusing of the pericardium and endocardium. This wall had a maximal thickness of 7 mm. The only area where muscular tissue was left was in the upper part of the left ventricle and a very small amount of its apex. The muscular wall of the right ventricle was somewhat hypertrophied and showed no signs of calcification. There was no gross pathological alteration in the valves, nor did the aorta or other arteries exhibit any atheroma or other changes.

SELWYN HEWITT, M.B., B.S., B.Hy., D.P.H.

Reviews

WOMANHOOD

The Psychology of Women. A Psychoanalytic Interpretation. Volume 2. Motherhood. By Helene Deutsch, M.D. (Pp. 439. 25s.) London: Research Books Ltd. 1947.

This volume is the second part of the author's psychological study of her own sex. She considers the adult woman and her reactions to all those events that lie in the province of the modern obstetrician and gynaecologist. Her study forms a branch of "psychosomatic" medicine, and though she presents it from the psycho-analytic viewpoint she does not mar it with the dogmatic assertions that sometimes emanate from that school. She acknowledges that many of the deviations from normal in the woman's sexual and maternal life are not readily explicable on purely physical grounds, and suggests that deep-seated mainly unconscious motives, acting through the autonomic nervous system and the endocrine glands, may be responsible for many of these anomalies. When well established they may be no more remediable by psychotherapy than by any other treatment. However, if the processes are understood, disorders may in some cases be prevented, and for that reason obstetricians will find the book worth reading.

The book begins with a study of the social position of women, with special reference to that of American women, whose importance and rarity in pioneering times led to their being highly valued. This natural esteem changed to a romantic and idealistic attitude towards them, which is only slowly fading. Women owe their complexity of character, and the many psychosomatic conditions to which they are subject, to the deep-seated conflicts between their erotic and maternal functions, neither of which can be entirely repressed, and between narcissistic tendencies to aggrandize themselves and altruistic impulses to sacrifice themselves for the sake of mate and child, especially child. Their masculine components likewise conflict with their feminine and may determine the course of their lives or influence it inconsistently. The oral component of their libido is directed externally in giving food and internally in the desire to make the child part of themselves. The author draws attention to the analogy in the unconscious mind between the sexual and digestive functions when discussing the reception of the sperm and the expulsion of the foetus and how these two components of the sexual cycle are separated by the whole period of pregnancy. She gives many examples of the influence of these conflicts on sexual intercourse, conception, pregnancy, parturition, lactation, the mother–child relationship, and the climacteric. She suggests that many cases of sterility, abortion, premature and delayed birth, difficulties in nursing, psychotic hostilities to husband and child in the puerperium and later, and the impulsive and inconsistent behaviour of the change of life are psychically determined. Similar conflicts determine the difficulties in the relationships of unmarried and adoptive mothers, foster-mothers, and stepmothers, and she draws attention particularly to the effects of emotional immaturity, emphasizing the similarities of reaction to these conflicts during puberty and the climacteric. Finally, she discusses the reactions of grandmothers sympathetically. This book deserves the attention of all medical men, whether general practitioners, psychiatrists, or gynaecologists. Although long, it is easy to read, and the interest is sustained.

R. G. GORDON.

ANTIBIOTIC THERAPY

Penicillin Therapy, including Streptomycin, Tyrothricin and other Antibiotic Therapy. By John A. Kolmer, M.S., M.D., F.A.C.P. Second edition. (Pp. 339; illustrated. $6.00.) New York and London: D. Appleton-Century Company. 1947.

The appearance of a second edition of a work on this subject is a reminder that penicillin has been with us for some time, and Prof. Kolmer is to be congratulated on his powers of digesting what is now a vast literature. He gives as many as 1,437 items in the list of references, and though the reader might have preferred them in alphabetical order he will be grateful for so comprehensive a guide to original sources. Prof. Kolmer has rearranged the book, now classifying disease regionally instead of aetiologically. In the earlier chapters, in which he considers general principles and methods, he still emphasizes the need for thinking in terms of bacterial species and not merely of the position and nature of the lesion. There is the usual list of species classified in three orders of susceptibility, and containing several disputable items—for example, *Proteus* and *Salmonella typhi* might well be promoted from the third ("slightly susceptible or insusceptible") to the second category ("moderately susceptible"), and *Actinomyces bovis* (hominis), *Erysipelothrix rhusiopathiae*, and *Streptococcus viridans* from the second to the first ("highly susceptible").

Has not the time come when the susceptibility of bacterial species to penicillin should be stated quantitatively instead of in these vague terms? Susceptibility to streptomycin is so stated in this book, although it is far more variable both intrinsically and according to the technique used for determining it. Reverting to the subject of *Salm. typhi*, we find that the author considers penicillin therapy to be ineffective or contraindicated in typhoid fever, and he appears to have overlooked the work of McSweeney and others on the treatment of this disease with penicillin and sulphathiazole given together in large doses. He commends penicillin esters in a passage that was evidently written before it was shown that human blood, unlike the mouse's, contains none of the esterase necessary for liberating penicillin from them. Practitioners in Britain who are exhorted by advertisements or compelled by circumstances to give large intramuscular doses only twice a day will find that Prof. Kolmer does not approve of this practice: the longest interval between doses considered advisable is four hours, except when oil suspensions are used.

This book is for the moment the most up to date and one of the most comprehensive guides to the use of antibiotics (the author also considers streptomycin, tyrothricin, and 14 others). It is a useful work of reference on obscure points and provides sound information on ordinary matters.

L. P. GARROD.

MIDWIFERY IN GENERAL PRACTICE

Postgraduate Obstetrics. By William F. Mengert, M.D. Drawings by Ruth Maxwell Sanders. (Pp. 398; 123 illustrations. 25s.) London: Hamish Hamilton Medical Books. 1947.

This book is written primarily for the general practitioner who does a certain amount of midwifery—attending, the author reckons, about 1,800 maternity cases during his lifetime. Prof. Mengert sets out to consider only those conditions whose frequency is not less than 1 in 2,000 deliveries. Nevertheless, he cannot resist mentioning a few others which, although interesting, are so rare as to be outside the experience of most practitioners. He omits nearly all theory and maintains a practical outlook throughout; there is little room for discussion, and his advice is of necessity dogmatically presented, sometimes in the form of a synopsis. Much of it is excellent, though it does not always conform to views generally accepted in Britain. Some of the methods of treatment described—e.g., the use of intrauterine bags in the treatment of placenta praevia—will be regarded as outmoded, and the technical details of caesarean section, vaginal hysterotomy, post-partum sterilization, biological tests for pregnancy, endometrial biopsy, tubal patency tests, and caudal anaesthesia are hardly of immediate interest to anyone engaged solely in domiciliary midwifery as practised nowadays.

A book of this kind has great possibilities; it requires a careful choice of subjects and a suitable placing of emphasis, and it is doubtful whether any two authorities would agree on them. Prof. Mengert has perhaps attempted too much in a small compass, with the result that his account of many subjects is superficial and unsatisfying. If he had restricted his field more severely and devoted more space and attention to the details of those things that really matter, we could recommend the book more strongly. As it is, some sections are very good and contain many useful practical tips. The author's common sense pervades the book, and his style makes it easy and entertaining reading.

T. N. A. JEFFCOATE.

PHYSIOTHERAPY

Massage and Remedial Exercises in Medical and Surgical Conditions. By Noël Tidy. Seventh edition. (Pp. 480; illustrated. 25s.) Bristol: John Wright and Son. 1947.

This book, which has reached a seventh edition in fifteen years, obviously satisfies a need, and we can commend it as a clear and trustworthy guide to the treatment of almost any disease by physiotherapeutic methods. Indeed, it is almost a short systematic account of medicine and surgery, including some pathology and not a little physiology and anatomy. We must criticize such statements as "anterior poliomyelitis is due to a *bacillus* as yet not definitely identified," or "the *bacteria* are carried by the lymphatics," and, a few lines later, "the *virus* first attacks the blood vessels of the anterior horns" (our italics). Such discrepancies are vestiges of the past and should be eliminated from future editions.

We wonder, after reading this book, whether physiotherapeutic procedures are not being used in unsuitable cases. For instance, we see an account of the application of these methods to the treatment of blood diseases—e.g., pernicious anaemia—and haemorrhoids, and the question comes to mind whether the interests of a large profession have not caused disease to become the handmaiden of massage rather than made massage serve the cure of disease. It seems that this branch of treatment, of such great benefit in appropriate cases, is showing signs of becoming a complete system of treatment, like osteopathy, naturopathy, and others. The wide scope of this book is likely to mislead the student into believing that there is scarcely any disease which should not be treated by the methods advocated. It would be unfortunate if this idea spread, for physiotherapy should be used only in certain cases and remain subservient to other forms of treatment.

This criticism of the general trend, however, does not apply to the book under review, which in itself is excellent. The extent to which such methods of treatment should be used is beyond the control of the author of a textbook of this kind, who has to meet a demand. Not a little of the blame for these tendencies lies with our own profession.

N. C. LAKE.

MANUAL FOR DIABETICS

Leitfaden für Zuckerkranke. By Dr. Georg R. Constam. (Pp. 127; illustrated. 12.50 Swiss francs.) Basle: Benno Schwabe and Co. 1947.

Close similarity combines with many subtle differences in the numerous books written by diabetic specialists for their patients: this is the most human ever written in the German language, optimistic and friendly. The author discusses all the usual details of diet, insulin injections, tests, and adjustments of treatment in a fairly simple fashion—clear enough, perhaps, to the universally intelligent Swiss but rather too detailed for our "hospital patient."

The food tables are probably the best available for the intelligent patient using a weighing machine. The author has designed them in the English tradition (Lawrence's schemes) and neglected the American Joslin methods, although he acknowledges the merits of both. The basis of his scheme is 10 g. of carbohydrate; in the tables he records the various weights of different foods containing this quantity, and ingeniously lists in another column the percentages of carbohydrate, protein, and fat contained in that weight of food. However, the figures often differ considerably from the values accepted in Britain for common carbohydrate foods (McCance and Widdowson), and he quotes no authority in support of this divergence. Though admirable for the highly intelligent patient, this book has too wide a scope and too much detail. The account of the treatment as well as the prevention of coma and gangrene is too full for the patient's understanding, yet not complete enough to help the medical man.

There are good illustrations of insulin bottles, syringes, the technique of injection, foot exercises, etc., and the production of the book is excellent. In this book there seem to be the seeds of two better ones—a shorter and simpler book for the patient, a longer and more detailed one for the medical practitioner treating diabetics.

R. D. LAWRENCE.

BOOKS RECEIVED

[Review is not precluded by notice here of books recently received]

The Electron Microscope. By V. E. Cosslett, Ph.D., M.Sc., M.A., F.Inst.P. (Pp. 128. 7s. 6d.) London: Sigma Books. 1947.

A popular account, including illustrations, of electron photomicrographs.

The Alchemist in Life, Literature and Art. By J Read, Ph.D., M.A., Sc.D., F.R.S. (Pp. 100. 10s. 6d.) London: Thomas Nelson and Sons. 1947.

A general account of alchemy by the Professor of Chemistry at St. Andrew's University.

Traité de Dietetique du Nourrisson. By M. Lust. (Pp. 539. 1,000 francs.) Paris: Masson et Cie. 1947.

A textbook of infant feeding.

Riflessi Sociali della Tonsillectomia. By Guido Calderoli. (Pp. 75. No price.) Bergamo: Carrara. 1947.

Certain aspects of the results of tonsillectomy.

Illustrations of Regional Anatomy. 7 Sections. By E. B. Jamieson, M.D. 7th ed. (£3 15s. for 7 sections; singly 12s. 6d.) Edinburgh: E. and S. Livingstone. 1947.

Coloured anatomical diagrams of the human body arranged in loose-leaf folders.

Cancer of the Breast. By D. C. L. Fitzwilliams, C.M.G., M.D., Ch.M., F.R.C.S., F.R.C.S.Ed. (Pp. 199. 25s.) London: William Heinemann. 1947.

A general account based on the author's experience.

Dermatology for Nurses. By G. H. Percival, M.D., Ph.D., F.R.C.S.Ed., D.P.H., and Elizabeth Toddie, S.R.N. (Pp. 116. 15s.) Edinburgh: E. and S. Livingstone, Ltd. 1947.

The nursing of patients with common skin diseases; illustrations, many in colour.

Good Health with Diabetes. By Ian Murray, M.D., F.R.F.P.S.G., F.R.C.P.Ed., and M. B. Muir, S.R.N. (Pp. 40. 2s.) Edinburgh: E. and S. Livingstone. 1947.

A manual of instructions for the diabetic patient.

Nelson Loose-Leaf Surgery of the Nose and Throat. Renewal pages. London: Thomas Nelson and Sons. 1947.

Biological Antioxidants. Transactions of the First Conference, Oct. 10–11, 1946, New York. Edited by G. C. Mackenzie. (Pp. 81. $2.) New York: Josiah Macy, Jr., Foundation.

Includes a number of papers on vitamin E in chemistry and biology.

Conference on Metabolic Aspects of Convalescence. Transactions of the 13th Meeting, June 10–11, 1946. Edited by E. C. Reifenstein, Jr., M.D. (Pp. 232. $2.) New York: Josiah Macy, Jr., Foundation.

Includes papers on male sex hormones, the adrenal cortex, and parenteral administration of fats.

Conference on Metabolic Aspects of Convalescence. Transactions of the 14th Meeting, Nov. 12–13, 1946. Edited by E. C. Reifenstein, Jr., M.D. (Pp. 190. $2.25.) New York: Josiah Macy, Jr., Foundation.

Includes papers on bone metabolism.

Traitement Chirurgical de la Tuberculose Pulmonaire. By Henry Joly. (Pp. 282. 820 francs.) Paris: Vigot Frères. 1947.

A general account of surgical measures for pulmonary tuberculosis.

Pictorial Handbook of Fracture Treatment. By E. L. Compere, M.D., F.A.C.S., S. W. Banks, M.D., F.A.C.S., and C. L. Compere, M.D., F.A.C.S. 2nd ed. (Pp. 390. $5.50 or £1 10s. 6d.) Chicago: The Year Book Publishers. London: H. K. Lewis. 1947

A profusely illustrated manual on the treatment of fractures.

Inky Way Annual, 1947–8. Edited by A. J. Heighway. (Pp. 204. 10s. 6d.) London: World's Press News Publishing Co., Ltd. 1947.

Entertaining contributions from many well-known journalists and cartoonists.

BRITISH MEDICAL JOURNAL
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THE DISCUSSION WITH THE MINISTER

As has already been announced the Minister of Health met the Negotiating Committee on Dec. 2 and 3. During the course of one afternoon and one morning the Minister went over the points made in a long document presented by the Committee, and the outcome of these discussions will soon be laid before the profession in the form of a statement which is expected from the Minister of Health at any moment now. The British Medical Association is sending to every doctor in the country, whether a member of the B.M.A. or not, a copy of the Negotiating Committee's statement together with a copy of the Minister's reply. For the purpose of record these statements will also be published in the *Journal* as well as the statement made by high legal authorities on the interpretation of Sections 35 and 36 of the Act. The Council of the B.M.A. is holding a meeting on Dec. 17 to discuss the present situation and to decide on future action.

THE TREATMENT OF PNEUMONIA

Twenty years ago no one would have ventured to predict that by the present time three separate forms of specific treatment for pneumonia would have been introduced, each of remarkable efficacy. The first of these, which held the field until towards the end of the last decade, was serum. Refined by Felton's method, latterly prepared in rabbits instead of horses, and ultimately made available for all the thirty then known types of pneumococcus, serum was shown to be capable of reducing the mortality of pneumonia by something like one-half. It may be noted in this connexion that during the war Erna Mörch,[1] working in Copenhagen, extended the list of known types of pneumococcus to over seventy, and the State Serum Institute catered for the serum treatment of infections by every one of these. But serum treatment calls for laboratory and other facilities which are available only in large centres, and its general application would have presented formidable difficulties. The second phase began with the introduction of sulphapyridine in 1938: this drug did all that serum had, and more, with the utmost facility, and rendered serum treatment almost obsolete within a year. The later sulphonamides have achieved equal or better results with much less liability to toxic effects, and if the last word had already been said at that stage there would have been little reason to complain. Yet a third remedy was still to appear, even more remarkable than the first two. Penicillin has two advantages over sulphonamides in the treatment of pneumonia, one of special and one of general application: it attacks pneumococci which are sulphonamide-resistant, and it is entirely free from any danger of serious toxic effects. On the other hand, when used in the conventional way it is much more troublesome to administer.

The present issue of the *Journal* contains four papers bearing on this subject. Two deal with the latest development of penicillin treatment, which is to obviate the difficulty and discomfort of injections by giving the drug by the mouth. Anderson and Landsman (p. 950), of Glasgow, the former with Ferguson[2] having previously found that there is little to choose between sulphonamides and intramuscular penicillin in the treatment of adult pneumonia, have compared intramuscular and oral penicillin in a further series of 90 cases, there being 45 in each group. A substantial proportion of the patients, actually greater in the oral group, had a bacteriaemia, which is the clearest possible indication that the series was of at least average severity. The doses used were moderate, the mean total amount used for each patient being only 800,000 units by the intramuscular and 1,650,000 by the oral route. This is by no means extravagant, and the oral dose used is less than that advocated by American authors. Perhaps administration in tablet form in milk and the restriction of fluid intake helped to render this smaller dose effective. As the authors remark, the relative achlorhydria of acute febrile states may also make for better absorption. At all events the results appear to have been excellent: there were only seven deaths in the whole series, all in cases complicated by other grave disease or moribund on admission, and in the duration of fever and the frequency of complications there is little to choose between the two groups. Suchett-Kaye and Latter (p. 953) treated twenty-five cases of pneumonia in infants by giving penicillin in the same form orally at 3-hour intervals, the individual dose varying from 10,000 to 40,000 units according to age. They record observations on the serum-penicillin levels attained, which though variable—as almost everyone has found in studying the effects of oral administration—were usually satisfactory. The results were good, except in four cases which were then treated successfully with sulphamezathine. Infants have a particular claim to oral penicillin, since they need comparatively little of the drug and should be spared the pain and disturbance of injections if possible. As the authors say, the possibility of using penicillin in this way is particularly valuable in circumstances in which injection treatment is actually impracticable.

Joules and Weller, of the Central Middlesex County Hospital (p. 947), have relied on sulphamerazine, at least for the primary treatment of the average case. It is not possible to assess the severity of their cases, and, in view of the dictum in an opening paragraph that in the absence of an influenza epidemic respiratory infections producing fever above 100° F. (37.8° C.) for more than one day have some degree of lung consolidation, it seems possible that they have detected radiologically a number of mild cases which might weight this series in favour of the treatment used. The only deaths, which appear to have been inevitable, occurred in patients treated with sulphamezathine or penicillin. The sulphamerazine-treated patients numbered 113, of whom 3 were also given penicillin from the start, while 27 others were given it later for various indications, such as failure to respond to the initial treatment, intolerance

[1] *Serological Studies on the Pneumococci.* Copenhagen. 1943.
Lancet, 1945, 2, 805.

of the drug, and the discovery that the infection was staphylococcal. Sulphamerazine has the advantage that adequate blood levels can be maintained by eight-hourly administration; the treatment is therefore simplicity itself, and involves the least possible disturbance to the patient. The possibilities of sulphonamide treatment are illustrated from an altogether different angle in the paper by Dr. David Lehr (p. 943), of New York, which was communicated to the International Physiological Congress in Oxford last July. This paper describes an extensive pharmacological study of the behaviour of mixtures of sulphonamides, from which it is clear that such mixtures overcome one of the principal dangers in the use of these individual drugs; further experience may show that the method has other advantages. The essential fact reported is that ingredients in such mixtures retain their individual solubilities in urine. It is thus possible by administering two or three drugs instead of one, each in a proportionally smaller dose, to reduce very greatly the danger of undue precipitation in the urinary tract. Careful studies on large numbers of animals also showed that these mixtures have a much lower toxicity than an equal dose of a single compound. It also appears that the blood levels attained are higher, owing to the better absorption of a smaller dose of each compound. Finally, clinical results have confirmed therapeutic efficacy and the rarity of crystallization in the urine, and it has been observed that allergic reactions are less common and nausea and vomiting are rare. From every point of view studied this combination of two or three drugs instead of one appears to offer decided advantages.

Which of these methods should now be used for treating a patient with pneumonia? It is right that every promising method should be tried, and reassuring to know that penicillin even when given by the simple oral route is a satisfactory remedy. Nevertheless it would, we think, be unfortunate if this became a routine treatment. It is more expensive, and might prove in more extensive trials to be less regularly reliable than the Glasgow findings suggest, owing to irregularity of absorption, a feature emphasized by all workers who have estimated blood levels and urinary excretion after administration by this route. Moreover, penicillin is a drug to which pneumococci can acquire some degree of resistance, which is then permanent. Would it not be a better policy to retain penicillin as a second line of defence, rather than to bring it into general use when an older and well-tried remedy will still serve so admirably, especially in its most modern forms? As Joules and Weller point out, many cases of pneumonia can satisfactorily be treated at home: the normal course of an average case responding to sulphonamide treatment is that of a two-day fever. If no such response follows, and if the case has unfavourable features from the outset, then hospital treatment is called for and other forms of chemotherapy may be necessary. Ideally the ultimate guide to specific treatment should be a careful examination of the sputum, including mouse inoculation if necessary, and determinations of the sensitivity of the pneumococcus or other organism found to whatever chemotherapeutic agents it is proposed to use. The finding of a sulphonamide-resistant pneumococcus would then call unequivocally for penicillin treatment, just as the finding of *H. influenzae* or *Bact. Friedländer* would contraindicate it. Penicillin has yet to find its true level. Its novelty and the romance associated with it create a popular demand which the profession should resist when necessary. A vogue for taking it by the mouth might prove an extravagance which we can ill afford.

AGENE AND CANINE HYSTERIA

The discovery by Sir Edward Mellanby[1] that flour bleached with "agene" produced hysteria in dogs has attracted widespread attention since its publication in the *Journal* at the end of last year. Veterinarians and others concerned with the health of dogs have been most directly interested, but the more important issue is the possibility that agenized flour may have some injurious effect on man. Since agene, a preparation of nitrogen trichloride, is regularly used in this country to improve the baking properties of flour, problems affecting both the public health and extensive interests in the milling industry may sooner or later have to be faced.

We published recently a further article by Mellanby[2] describing his attempts to find out why agene causes flour to become toxic and to identify the toxic factor. Agenized flour was washed free from starch with water, and the resulting gluten was found to produce hysteria in dogs. Gluten prepared from untreated flour did not cause hysteria. At first sight this would seem to prove that some product made from the protein fraction of the flour is the toxic agent. It is well known, however, that gluten so prepared contains most of the fat originally present in the flour, and that the fat of agenized flour contains chlorine derived from the nitrogen trichloride. The gluten of agenized flour was therefore extracted with a mixture of alcohol and ether. When given to dogs the defatted gluten still caused hysteria, while the fatty extract was harmless. An attempt was then made to identify the fraction of the protein made toxic by agene. For this purpose agenized gluten was extracted with 65% alcohol, and so divided into a soluble "gliadin" fraction and an insoluble "glutelin" fraction. Both fractions caused hysteria, but gliadin appeared to be more toxic than glutelin.

Mellanby's observations have now been confirmed and extended by Dr. T. Moran,[3] director of the Research Association of British Flour Millers. From a consideration of the chemical behaviour of nitrogen trichloride, and from a study of its quantitative effects in changing the acidity of dough, he has concluded that though some of the chlorine liberated by this compound is used for oxidation a substantial proportion combines chemically with the constituents of the flour, either by addition or by substitution. Microbiological tests show that the process of agenizing flour does not affect any of the better-known members of the vitamin B complex, and, in particular, that there is no loss of pyridoxin (vitamin B_6). Lack of this vitamin had previously been suggested as a possible cause of hysteria[4] in dogs in view of the observation by Chick, El Sadr, and

[1] *British Medical Journal*, 1946, **2**, 885.
[2] Ibid., 1947, **2**, 288.
[3] *Lancet*, 1947, **2**, 289.
[4] *British Medical Journal*, 1946, **2**, 903.
[5] *Biochem. J.*, 1940, **34**, 595.

Worden[5] that its deficiency causes epileptiform fits in rats. Even stronger evidence that a toxic agent rather than dietary deficiency causes canine hysteria was obtained by giving dogs very heavily agenized flour: 80 mg. of agene was added to each 100 g. of flour, as compared with the 6.4 mg. usually added in routine milling. After a single meal containing flour so treated, dogs developed hysteria within twenty-four hours, obviously much too soon for the development of a deficiency syndrome. Cures were readily effected in a few days by giving untreated flour. Hysteria was provoked in five days by flour treated with 20 mg. of agene per 100 g., and in about the same time by flour which had been treated with 80 mg. of agene and then diluted with three times its weight of untreated flour. The toxic factor was found not to be extracted by water or by fat solvents, which is in agreement with Mellanby's work. Moreover it was again located in the gluten fraction, and on fractionation with 70% alcohol both the soluble and insoluble fractions were found to be injurious.

In his next experiments Moran attacked the problem from a new standpoint and demonstrated clearly that the development of toxicity after treatment with agene is not peculiar to proteins derived from wheat. When dogs were given agenized casein they had hysteria within twenty-four to forty-eight hours. Similar results were obtained with agenized zein, the protein of maize, while with agenized gelatin slight hysteria occurred after ten days. The result with zein is interesting, because this protein is devoid of the amino-acids glycine, tryptophan, and lysine. If toxicity is caused by the action of agene on a specific intramolecular grouping in protein it is clear that these three amino-acids cannot be involved. Another significant point on which Mellanby and Moran agree is that even heavy treatment with free chlorine does not produce in flour whatever changes are responsible for canine hysteria.

In his earlier paper Mellanby[1] contended that agene makes flour injurious by the production of a toxic agent rather than by the destruction of some essential nutrient. These recent developments have fully confirmed this conclusion, though it remains to be decided whether agenized flour is the only, or even the most important, cause of canine hysteria. The identification of the toxic agent in the near future should not unduly tax the skill of the organic chemist and should help us to answer the crucial question whether or not agenized flour is harmful to man. In the meantime any feeling of security based on the previous conclusion that animals other than the dog are not susceptible to agene poisoning may be somewhat shaken by Mellanby's recent experience with ferrets. This animal, he has found, develops unmistakable symptoms of hysteria when fed upon agenized but not when fed on untreated flour.

ADDISON'S DISEASE IN PREGNANCY

Addison's disease associated with pregnancy is an interesting but rare combination. In 1922 Fitzpatrick[1] summarized eleven cases from the literature and described a personal case. In 1945 van Zwanenberg[2] reported two cases and referred to another fourteen collected from the literature. He concluded, as did Fitzpatrick, that the prognosis is bad. Of the 13 cases for which details were known, 7 ended fatally for the mother, and in 6 the baby was born dead. All the maternal deaths occurred during the puerperium, at which time most cases showed a tendency to an Addisonian crisis. Abortion or the induction of labour did not appear to help, but the two patients who received adrenal cortical extract immediately after labour did not suffer a puerperal crisis. Many of the cases referred to by Zwanenberg date back many years and probably did not receive what would now be regarded as adequate treatment for adrenal cortical failure. Indeed it seems likely that in this disease, as with so many others, the complication of pregnancy becomes increasingly less serious as more efficient methods of treatment are discovered, and, in general, it is best to treat the disease and not to interfere with the pregnancy. This suggestion is borne out by recently published reports of three further cases. Murphy[3] tells of a woman treated for Addison's disease by subcutaneous implants of desoxycorticosterone acetate with such good effect that she was well enough to marry and become pregnant. There was no evidence that pregnancy itself had a beneficial effect on the disease, nor was there any reason to believe that it had an adverse influence or that the maintenance dose of desoxycorticosterone had to be increased. Labour was induced because it had not begun three weeks after the calculated date; it then progressed easily and rapidly. The baby was stillborn as a result of multiple looping of the cord round the neck and axillae. In the case described by Samuels, Evans, and McKilvery[4] the condition was also brought under control by implants of desoxycorticosterone before conception took place. Desoxycorticosterone, 6 mg. daily, was given during most of the pregnancy, but the authors consider this was probably unnecessary. There was some evidence that pregnancy had a beneficial effect on the patient, but after delivery Addisonian symptoms recurred and necessitated careful treatment. Estimation of the 17-ketosteroid excretion showed a rise about the sixth month which was maintained until delivery, when the level dropped to what it had been before the pregnancy. It is suggested that this increased output and the improved condition of the patient were due possibly to the action of the foetal adrenals. A compensatory action on the part of foetal ductless glands has often been postulated in the case of other endocrine disorders such as diabetes mellitus. So far as Addison's disease is concerned the evidence is as yet far from conclusive, and in only one of the patients referred to by Zwanenberg was the condition said to be improved by pregnancy. The occurrence of Addisonian crises soon after delivery is perhaps in favour of the idea, although the stress of labour might be an important factor. The normal adrenal cortex undergoes hypertrophy during pregnancy, so an alternative explanation of occasional observations suggesting that pregnancy has a beneficial effect on Addison's disease could be based on the supposition that remaining small areas of healthy gland undergo hypertrophy. If this were true, however, it might be expected that the good effects of pregnancy would persist for a longer time after delivery and that crises would not occur so early in the puerperium, particularly as in some animals adrenal hypertrophy is even more noticeable in the puerperium than in pregnancy.[5,6]

S. L. Simpson,[7] who mentions two patients with Addison's disease who survived pregnancy, describes in detail a third case in which the patient had two pregnancies, each resulting in a live child. He emphasizes a feature noted by

1 *Surg. Gynec. Obstet.*, 1922, **35**, 72.
2 *St. Bart's Hosp. J.*, 1945, **49**, 31.
3 *Proc. roy. Aust. Coll. Phys.*, 1946, **1**, 69.
4 *Endocrinology*, 1943, **32**, 422.
5 Venning, Eleanor H., Ibid., 1946, **39**, 203.
6 Teppermann, J., Engel, F. L., and Long, C. N. H., Ibid., 1943, **32**, 373.
7 *Proc. roy. Soc. Med.*, 1946, **39**, 511.

other writers—namely, that pregnancy may precipitate the onset of symptoms of Addison's disease, due presumably to the increased demands made on the adrenals. Moreover, in his case the patient failed to lactate on both occasions. This observation tallies with the results of animal experiments in which it has been shown that bilateral adrenalectomy inhibits lactation unless it is followed by the administration of adequate amounts of adrenal cortical extract. In Simpson's case the regular administration of desoxycorticosterone and sodium chloride during the second pregnancy and puerperium did not bring about lactation, so it would appear that some other cortical factor is necessary. It is noteworthy that in none of the reported cases, irrespective of their treatment, was the uterine action in labour disturbed.

HORMONE TREATMENT OF CANCER OF THE BREAST

Since the original reports[1 2] in this country on the occasional clinical retrogression of carcinoma of the female breast after the administration of stilboestrol little has been added to our knowledge of the carcinostatic effect of the sex hormones. A recent paper from New York[3] reports the administration of ethinyl oestradiol, a synthetic oestrogen, to 17 patients suffering from mammary cancer. This account shows how inadequate are our yardsticks for estimating the retrogression of human tumours. There is no available method of measuring with reasonable accuracy the volume of even an accessible tumour, and clinical estimates of increase or decrease in size are notoriously fallacious. Only complete disappearance can be accepted as clear proof of a decrease in size.

Certain dramatic qualitative phenomena, however, are acceptable as evidence of retrogression, and these were sometimes seen in the series described by Herrmann and his co-workers. A decrease in size of pre-existent carcinomatous ulcers was observed in two cases and graphically recorded, and there was complete healing of an ulcer in a third case. A decrease in the size of pulmonary metastases was measured radiographically in two cases. A protuberance photographed in profile had flattened out after two months' treatment. In no case did the primary tumour or a metastasis completely disappear. Serial biopsies showed no alteration in the histological or cytological pattern of tumours that appeared to regress under treatment. The microscopical picture altered after treatment in only one tumour, and that increased in size during treatment. In one patient the breast tumour increased in size and fungated rapidly at the very time when a pulmonary metastasis from it appeared to be shrinking.

The authors consider that there was a favourable response in 7 of the 17 cases, and this response was obtained for the most part in women over 60 years of age. In young women oestrogen therapy actually appeared to hasten the growth of the tumour. Of the 17 patients 7 died of the disease, and one of coronary occlusion, within eighteen months of starting treatment. Of the 7 patients who died 5 were under 60 years of age; indeed no patient under 60 years of age survived for longer than eighteen months. This series is a small one, but patients selected for oestrogen therapy are necessarily those who are unsuitable for operation or for radiotherapy or whose disease is resistant to these other forms of treatment. In this sense it is gratifying that their numbers are relatively few and that substantial series are therefore slow to accumulate.

[1] Discussion, *Proc. roy. Soc. Med.*, 1944, **37**, 731.
[2] Haddow, A., Watkinson, J., and Paterson, E., *British Medical Journal*, 1944, **2**, 393.
[3] Herrmann, J. B., Adair, F. E., and Woodard, H. Q., *Arch. Surg.*, 1947, **54**, 1.

DRUG ADDICTION

In a comprehensive review[1] of the many therapeutic difficulties presented by the drug addict we are early reminded that addiction is a manifestation of a morbid state and that the victim must be treated as a patient. It is a mistake to apply the term "drug addiction" to all cases in which drugs cause euphoria. The cocaine habit is often just an indulgence in vice rather than a state of true addiction; the taking of cannabis always falls into the former category. For a proper understanding of the state of addiction it is well to refer to Himmelsbach's definition of what he terms a "physical dependence." This is an acquired abnormal state wherein the regular administration of adequate amounts of a drug has, through previous prolonged use, become indispensable for physiological equilibrium. The demonstration of this state can be made only by withdrawal and the production of withdrawal symptoms. They are classified as (*a*) mild: yawning, lacrimation, sneezing, sweating; (*b*) moderate: tremor, gooseflesh, anorexia, mydriasis; (*c*) marked: pyrexia, rise of respiratory rate and systolic blood pressure, insomnia, restlessness; (*d*) severe: vomiting, diarrhoea, loss of weight.

Not every person who takes a habit-forming drug is a drug addict. Only 19% of patients admitted to the Narcotic Hospital in Lexington were found by Himmelsbach to be really dependent on drugs to an extent sufficient to render their cases suitable for study. It is suggested that many alleged addicts have merely a mild drug-habit with only slight physical dependence. This may be due in great part to the adulteration of supplies by "dope pedlars," and to the recurrent difficulty in obtaining opiates. The importance of the foregoing is that accurate appraisement of the category to which the patient belongs must precede assessment of treatment. Thus a chronic morphine addict habituated to the drug given therapeutically can be much more readily detoxicated if the therapeutic indication has disappeared than can the morphine addict who is predisposed to addiction and whose unstable mind leads him to search for euphoria. The distinction is not always easy to make, because a potential addict may in fact become one owing to the development of a disease requiring morphine.

The need to consider prophylaxis is emphasized by the statement that no person is immune to opiate addiction; if morphine is given to 100 people regularly for a certain time it will produce abstinence symptoms in all of them. In many countries prophylaxis is already carried as far as can reasonably be expected: control of the sale of drugs and the limitation of their use to doctors, dentists, and veterinary surgeons are governed by stringent regulations. It is suggested that more could be done in the direction of educating doctors to use euphoric drugs only when the simple analgesics fail, and then to aim at an initial dose which while sufficient to relieve pain will not be large enough to cause euphoria. Morphine suppositories are said to have the same therapeutic effect as injections, and should be preferred. Against this it might well be argued that a patient will quickly link the suppositories with relief of pain; furtive self-administration would be simplified for the addict, and nursing attendants would be as likely to use them as an injection. The prescription of cocaine, except for direct application by a surgeon, is never justified. There is no risk in refusing cocaine to an addict, because, in contrast to the use of morphine, dangerous abstinence effects never occur, even in the severest cases.

In treating those addicted to opium and its derivatives it is generally agreed that rapid withdrawal is correct. Institutional treatment is essential. The doses of the drug should be so reduced as to avoid serious withdrawal

[1] *Bull. Hlth. Org. L. o. N.*, 1945–6, **12**, No. 4.

symptoms. The aim should be to stop the drug in ten days. More prolonged withdrawal is no more bearable to the patient, while it certainly prolongs the discomfort, and this leads only too often to his discharging himself. This raises the question whether a law for compulsory treatment should not be enacted. Personal liberty for an addict whose mind is warped by craving is hardly in the public interest.

The report recognizes the existence of morphinists and opium eaters who appear to be in an "arrested development" stage of addiction. They remain addicted to small and constant doses of the drug, and are efficient and healthy. Stopping the drug makes them ill and incapable of work. Treatment of this group is unnecessary, and possibly dangerous in that it may lead to true and progressive addiction. The greater part of the report is devoted to a detailed consideration of the methods of cure, and pours a salutary cold douche on the many claims for dramatic cures without tears. This work is admirably compiled and worthy of detailed study by those who may be given the responsibility for the cure of a drug addict. It is the last number of the *Bulletin of the Health Organization of the League of Nations*. Its successor will be the *Bulletin of the World Health Organization*.

THE TREATMENT OF MYASTHENIA GRAVIS

Although thymectomy has produced dramatic improvement in some cases of myasthenia gravis,[1] and the experimental use of diisopropyl fluorophosphonate has opened up a new field, there are still many patients who continue to get relief from "prostigmin." This substance and others which may enhance its effect form the basis of the medical treatment of the disease. It was in 1936 that Dale, Feldberg, and Vogt[2] showed how acetylcholine is released at voluntary nerve endings when a volley is discharged down the motor nerve. Previously Mary Walker[3] had used physostigmine with striking success in a case of myasthenia gravis, because the disease closely resembled curare poisoning, for which physostigmine was known to be an antidote. Since then its derivatives have been employed, the most successful being prostigmin or "neostigmin"[4] and also neostigmin methyl sulphate.[5] Ephedrine[6] may be given as well with advantage in some cases, and guanidine has also been found helpful.[7] Froke, Margoshes, and Harrell[8] tried guanidine in doses of 25 mg. per kilo of body weight in association with prostigmin and found that subjectively, and also on measurement of the myasthenic response with a recording ergograph, there was material improvement in the patient's muscular efficiency.

It is generally recognized that in myasthenia gravis there is a disorder of the acetylcholine mechanism at the myoneural junctions, but its exact nature is still unknown. Froke and his co-workers have analysed the possibilities. The first, that cholinesterase, which breaks down acetylcholine into choline and acetic acid, is present in excessive amounts, was discounted by the work of Cooke and Passmore.[9] The second, that acetylcholine is not liberated, is ruled out by the action of prostigmin, which merely prevents its destruction. The third is that acetylcholine is found in abnormally small amounts. This might be due to lack of precursor substances, lack of potentiator substances, or excess of inhibitor substances. This possibility is supported by the observations of Torda and Wolff,[10] who found that the serum of myasthenic patients only produced one-third the amount of acetylcholine synthesized by normal serum in the presence of frog's brain *in vitro*. It is also supported by the direct observation of the effects of prostigmin and acetylcholine in varying amounts in myasthenic patients compared with normal subjects. The last possibility is that the myasthenic muscle fibres might be less sensitive to the action of acetylcholine than those of normal subjects, but there is no doubt that the muscles in myasthenia are unusually sensitive to acetylcholine injected directly into an artery. Minot[7] considered that such might be the reason for any potentiating action which guanidine might have on prostigmin, and it is possible that guanidine makes myasthenic muscle fibres contract more efficiently in the presence of prostigmin. If it does, it will enable a smaller effective dose of prostigmin to be given, as suggested by Froke, Margoshes, and Harrell, but it must be remembered that its use in the muscular dystrophies, which was based on a similar theory, proved disappointing.

[1] Blalock, A., *J. thorac. Surg.*, 1944, **13**, 316.
[2] *J. Physiol.*, 1936, **88**, 353.
[3] *Lancet*, 1934, **1**, 1200.
[4] Walker, M. B., *Proc. roy. Soc. Med.*, 1935, **28**, 759.
[5] Viets, H. R., *Amer. J. med. Sci.*, 1944, **208**, 701.
[6] Edgeworth, H., *J. Amer. med. Ass.*, 1940, **94**, 1136.
[7] Minot, A. S., Dodd, K., and Riven, S. S., *Science*, 1938, **87**, 348.
[8] *N. Carolina med. J.*, 1946, **7**, 462.
[9] *Quart. J. Med.*, 1936, **5**, 21.
[10] *Arch. Neurol. Psychiat.*, 1944, **52**, 554.

AT THE BASE OF THE DUODENAL CAP

Duodenal ulcers occur so commonly that physicians may be forgiven if they get into the habit of attributing to ulceration all deformities of the duodenal cap seen on radiological examination. Other conditions which deform the duodenal cap, though they may be uncommon, should nevertheless be considered; their symptoms may be similar, but they often require different treatment; and the prognosis may be very much better. Hypertrophic pyloric stenosis occasionally occurs in an adult, either as a new condition or because it has persisted from infancy. Katz[1] has recently recorded two examples, of which one falls into the latter group. He agrees with other observers that the radiological appearances in this disorder—crescentic indentation of the base of the duodenal cap, narrowing of the pyloric canal, and hyperperistalsis—are not pathognomonic. Laparotomy should always be undertaken in these cases, for a similar picture may be seen in carcinoma of the stomach.

Prolapse of redundant gastric mucosa into the duodenum is another unfamiliar condition, though Scott,[2] in reporting 14 cases observed during 1,346 successive *x*-ray examinations of the upper gastro-intestinal tract, maintains that it is not rare. The symptoms may be indistinguishable from those of peptic ulceration, but Appleby[3] considers that there is usually intermittent cramping pain aggravated by food and relieved by vomiting. Though the precise diagnosis of a prolapse of the gastric mucosa into the duodenum can only be suspected from the history, both these authors consider that it can be established by radiology. However, there is some difference of opinion about this: whereas Scott considers that the characteristic picture is that of a central "mushroom" or lobulated "cauliflower-like" negative shadow, Appleby shows that the usual appearance is of a "jockey-cap" type of filling defect together with a normal mucosa. Again, while Scott reports successful results from a local resection of the extra mucosa, Appleby advocates gastrectomy. Whichever procedure is best it is certain that the prolapse may occasionally be so great as to constitute an intussusception of the gastric mucosa with symptoms of obstruction. Eckhoff[4] described such a case; it was successfully treated by local resection of the mucosa.

[1] *Amer. J. digest. Dis.*, 1947, **14**, 85.
[2] *Radiology*, 1946, **46**, 547.
[3] *J. int. Coll. Surg.*, 1947, **10**, 135.
[4] *Guy's Hosp. Rep.*, 1943, **92**, 38.

THE DANGERS OF GOING TO BED

BY

R. A. J. ASHER, M.D., M.R.C.P.

It is always assumed that the first thing in any illness is to put the patient to bed. Hospital accommodation is always numbered in beds. Illness is measured by the length of time in bed. Doctors are assessed by their bedside manner. Bed is not ordered like a pill or a purge, but is assumed as the basis for all treatment. Yet we should think twice before ordering our patients to bed and realize that beneath the comfort of the blanket there lurks a host of formidable dangers. In "Hymns Ancient and Modern," No. 23, Verse 3, we find:

> "Teach me to live that I may dread
> The grave as little as my bed."

It is my intention to justify placing beds and graves in the same category and to increase the amount of dread with which beds are usually regarded. I shall describe some of the major hazards of the bed. There is hardly any part of the body which is immune from its dangers.

Respiratory System.—The maintenance of one position allows the collection of bronchial secretions, which, stagnating in the bases, encourage the development of hypostatic pneumonia. Further, the absence of exercise and the diminished respiratory excursion consequent on bed rest prevent the re-expansion of collapsed or diseased lung.

Blood Vessels.—Thrombosis and thrombo-embolism are some of the most disabling and lethal catastrophes that bed rest can bring to a patient. The absence of leg movements means that the venous blood lacks the helpful squeeze from the muscles which normally speeds its flow, and the flexion of the thighs (particularly when there is Fowler's position or a knee pillow) obstructs it the more. One theory of phlebothrombosis is that it starts with endothelial damage caused by the weight of the leg on the bed compressing emptied calf veins. Thus it may well be said that thrombophlebitis is the internal counterpart of the bed-sore. We may one day regard a thrombosis to be as much a sign of nursing mismanagement as we do the ordinary bed-sore to-day. It is significant that Hunter, Sneedon, and others, performing post-mortem examinations of the veins of the calf in middle-aged and elderly people who had been in bed a considerable time, found thrombosis of the calf veins in 53% of the cases.

Skin.—The frequency and dangers of bed-sores are too well known to need much comment. A large bed-sore in a heavy patient, especially an incontinent one, is a nightmare to the nursing staff, and the pressure points on the heels are often a source of great pain and misery to the patient even if the skin is still unbroken.

Muscles and Joints.—The contraction of some muscles and the stretching of others are complications of rest which may cause considerable crippling. Foot-drop is of course the commonest, and stiffness and flexion of the knee-joints probably the next. The weakness and wasting of the general skeletal musculature and the restriction of the excursion of the joints are often manifest in the hobbling, painful gait of the convalescent patient.

Bones.—When bones are not used the calcium drains from them, and this disuse osteoporosis can be a serious matter, especially in the elderly. Fractures for that reason may take longer to heal, and the absence of weight-bearing is another reason for delayed union. This is shown by George Perkins's recently published cases where the broken ends of bone, when splinted by a metal plate, did not heal until the plate accidentally broke and the resulting increase in weight-bearing led to rapid bony union. The advantages of the Smith-Petersen pin over older methods of managing intracapsular fractures of the femur are largely due to the shorter time in bed.

Renal Tract.—The drain of calcium from the bones that I have just mentioned causes an increased liability to urinary calculi, and both kidney and bladder stones are sometimes in part due to bed rest. Far commoner than this is retention of urine. A patient, particularly a male, with a perfectly normal urinary tract can find difficulty in using a bottle—probably because of the horizontal position of the body coupled with the nervousness and embarrassment felt on attempting this unnatural, uncomfortable, and unfamiliar method of micturition. In older people this difficulty may lead to acute retention with overflow or to simple incontinence. Bed-sores may develop and keep the patient to bed, so initiating a vicious circle of bedridden incontinence. Prolonged incontinence leads to a deterioration of hygienic morale, and a patient may continue to be incontinent from sanitary sloth rather than urological disease. Getting a patient out of bed may turn him from an incontinent person to a clean one.

Alimentary Tract.—This too is not immune from the bad effects of rest in bed. After a few days minor dyspepsias and heartburn may be noticed; the appetite is often lost. Constipation occurs almost invariably, and even if not of grave significance is often a grievous worry to the patient. Its causes are, first, the absence of muscular movement; secondly, the change of environment (no one can say why this causes constipation, but it does); and, thirdly and most important, the difficulties of evacuating the bowel in a hospital bed-pan. On a bed-pan the patient is unable to use his abdominal muscles and his nearness to fellow-patients discomforts him. Precariously engaged in balancing himself, he sits there, poised unhappily above his own excrement in great dissatisfaction and distress. The constipation of bed rest is most harmful in the aged, where retained scybala may lead to a diarrhoea which marks the underlying obstruction. Retention with overflow is nearly as common at the back as in front. Quite often complete intestinal obstruction can develop from retained faeces, and when enemata fail to shift the scybala digital removal has to be practised—a procedure as unpleasant for the evacuator as for the evacuee.

Nervous System.—It is well known that, particularly in the ataxic diseases such as disseminated sclerosis or tabes dorsalis, even a short spell in bed may produce a deterioration of mobility which takes weeks to overcome, and any length of time in bed may leave a patient bedridden many years before the natural course of the disease would have made him so.

Mental Changes.—Lastly, consider the mental changes, the demoralizing effects of staying in bed. At the start it may produce fussiness, pettiness, and irritability. The patient may acquire an exaggerated idea of the seriousness of his illness and think, "Surely I must be very ill if I am kept in bed?" At a later stage a dismal lethargy overcomes the victim. He loses the desire to get up and even resents any efforts to extract him from his supine stupor. The end result can be a comatose, vegetable existence in which, like a useless but carefully tended plant, the patient lies permanently in tranquil torpidity.

Even the insomnia and nocturnal restlessness so common in hospital patients may be related to the abuse of rest. Too much sleep during the day means too little sleep at night. You may notice that many patients who disturb the ward at night are flat on their backs snoring during the day. They lie in bed with nothing much to do, and we cannot blame them for taking frequent cat naps. I am sure that many hours of half-sleeping and dozing are less beneficial than a few hours of deep sleep, and I believe they encourage a certain confusion of mind.

So much for the commoner hazards of the bed. There are many I have omitted. I have not mentioned the loss of education in children who are long in bed, nor spoken of the dangerous dust that arises during bed-making, but even those evils I have outlined may help to show that rest in bed is anatomically, physiologically, and psychologically unsound. Look at a patient lying long in bed. What a pathetic picture he makes! The blood clotting in his veins, the lime draining from his bones, the scybala stacking up in his colon, the flesh rotting from his seat, the urine leaking from his distended bladder, and the spirit evaporating from his soul.

I have painted a gloomy and unfair picture: it is not as bad as all that. There is much comfort and healing in the bed, and rest is essential in the management of many illnesses. My object has been to disclose the evils of *over*dose, and I want now to indicate briefly how some of them may be avoided or overcome.

First, bed rest should be prescribed and not assumed—that is to say, a sister should not confine the patient to bed without the doctor's ordering it. Secondly, doctors should revise their attitude to rest where it is unsound. In a chronic ward of which I once had charge I found a lady who had been in bed for 17 years with a diagnosis of nervous debility and whitlow. She had survived this remarkable hibernation with little damage, and though she was very upset when I ordered her up she became a different person when she was fully ambulant. It may well be, too, that our attitude to rest in more acute cases could be modified. Rheumatic-fever cases are often kept flat on their backs for a considerable time, although there is no evidence that this modifies the incidence of heart complications and there *is* good evidence that the work of the heart is increased by the supine position. Patients with coronary thrombosis traditionally have six weeks in bed, but the evidence that this diminishes the incidence of complications is slender. Indeed, Sir James Mackenzie, who had frequent angina after cardiac infarction in 1908, never spent more than a few days in bed, but continued playing golf till his exercise tolerance at last became too small. He lived an active and useful life for 17 years after his first attack.

John Powers, of Cooperstown, New York, reported on 100 consecutive patients who were allowed to sit in a chair and walk on the first day after major operations. He compared them with an equal number who remained in bed for 10 to 15 days and found fewer complications in the first group. Further, the early ambulant cases were back at work within 4.8 weeks as compared with 8.7 weeks in the control group. All these facts encourage us to review the traditional amounts of bed rest that we order our patients.

The third way of avoiding the dangers of bed lies in altering the equipment and arrangement of a ward. There should be a day-room attached to every ward and lockers for patients to keep their ordinary clothes in. Too often a sister puts all her patients back to bed as a housewife puts all her plates back in the plate-rack—to make a generally tidy appearance. Too often patients stay in bed because, shuffling round in slippers and dressing-gown, they are cold and uncomfortable. They would welcome a warm day-room with chairs and books. Some heart cases ought to be allowed to spend most of the day in arm-chairs and to sleep the night in them if they feel much more comfortable that way. For those that have to be in bed a commode might be allowed as an alternative to a bed-pan in most cases. More liberal attention should be paid to breathing exercises, limb-moving, and occupational therapy both to prevent complications and to distract the patient from going to sleep out of sheer boredom.

> "Teach us to live that we may dread
> Unnecessary time in bed.
> Get people up and we may save
> Our patients from an early grave."

THE ANATOMY OF SPEECH

HUXLEY LECTURE

The Huxley Memorial Lecture was delivered before the Royal Anthropological Institute on Nov. 25 by Dr. W. L. H. Duckworth, of Jesus College, Cambridge. Dr. Duckworth's subject was "Some Complexities of Human Structure," and he took as his text the remark of Huxley in 1865 that anthropology was the science which unravelled such complexities. He confined his review to the organs of speech and the parts of the brain with which speech is associated.

Lips and Tongue

Employment in the production of articulate speech was not the only function performed by the lips; they still played a part in gesture, of which use the South African bushman provided a good example. In spoken and gesture language alike the agents used were the facial muscles. Some eight or nine muscles converged on each side of the two angles of the mouth, where they merged in an area specially responsive to traction exercised by muscle fibres. One group of the muscles concerned was the so-called labial tractors, consisting of fibres entering the substance of the lip almost perpendicularly, from above or below. Some of these fibres penetrated not only the peripheral fibres of the orbicularis oris but the marginal fibres as well; such penetration was said to provide a contrast between human lips and those of the chimpanzee, in which the marginal fibres were barely reached. The variety of movements around the aperture of the mouth was no less important than the variety of parts found in the mechanism. These movements were essentially skilled, and it was permissible to suppose that in future they would become very much more skilled than at present.

Comparison of the tongue in the various types of mankind rested mainly on observations of the sensory papillae distributed over its surface. The papillae combined in lines to reproduce the letters V or Y, but the angle at which the divergent arms of the letter were inclined to one another was subject to considerable variation and to interruption. The tongue, like the lips, could be protruded and withdrawn, and comparative anatomy suggested that these movements appeared early in the evolutionary history of the tongue or its representatives. The connexions both of the intrinsic and extrinsic muscles deserved further exploration. More than half a century ago Macalister declared that there was reason to believe that the musculature of the tongue varied in different races—a statement which did not seem to have been disproved.

Lower Jaw, Soft Palate, and Larynx

The lower jaw had been very fully studied. In articulated speech the movements of the jaw evidently involved certain muscles whose study was inseparable from that of the bone itself. Some of these muscles made no direct connexion with the tongue, while others entered the substance of the tongue as its extrinsic muscles. The lecturer added that evaluation of the human lower jaw had not been rendered more simple by acquiescence in the view that the Piltdown mandible belonged to an individual whose brain, as inferred from the skull, suggested, if it did not prove, endowment with human speech.

The soft palate combined with the hard palate and the tongue in contributing to the production of speech. Its tendency to assert its existence in snoring was almost pathological. Study of comparable sections from the soft palate of an Australian aboriginal and an African negro had not so far provided any suggestion of specific peculiarities.

The larynx appeared to be simply constructed, but its parts were numerous. The intersection and interlacement of the fibres of the thyro-arytenoid muscles were now known to be much more complex than was previously believed. The importance of the muscle was evident in view of its close relation to the vocal fold, for it was thus at the very source of sound production in the larynx.

Reviewing these various vocal organs as a whole, the lecturer said that it was worth while inquiring whether they displayed any similarity in their structural complexity. In the lips, the soft palate, and the vocal folds alike muscular fibres were conspicuous, and with a slight exception all were of the striate variety. In each instance they tended to surround a passage or cavity the width or dimensions of which they varied by their action or relaxation. The tongue was different in some respects, but it would not be impossible to present the tongue as an example of extraordinary specialization of the muscular tissue surrounding the cavity of the mouth, while as to the mandible this was an ossification in a great sheet of muscle stretching from one temporal region to the other. While a general agreement of scheme might thus appear, a marvellous amount of differentiation accompanied it.

Speech Centres

Turning finally to the parts of the brain associated with speech, Dr. Duckworth spoke particularly of two areas in the left cerebral hemisphere (in right-handed persons), namely, on the frontal lobe, mainly in front of the central sulcus, and on the parietal lobe, comprising the supra-marginal, angular, and posterior parietal convolutions. Disintegration of the first of these areas affected speech strongly, if it did not always abolish it. There was failure to co-ordinate the contributions of the lips, tongue, and soft palate, and vocalization became a continuous cry or grunt, not controlled by the patient. Persons suffering from disease of the left posterior parietal

convolution could speak, but were likely to talk nonsense and to be unable to comprehend spoken or written language. The first area was concerned with the co-ordination of muscular actions, the second with comprehension of things seen or heard or the impressions of muscular sense. In both areas the human brain exhibited structural features indicating progress in advance of the highest apes, and, in regard to the second area, a much higher development than in other animals.

The organs he had reviewed, said the lecturer in conclusion, were common to mankind and to a large number of animals. Detection of distinctive human characteristics was comparatively easy when the countenance or the brain were in question, but other parts called for the knowledge furnished by dissection and the study of microscopical preparations. With this assistance, systems such as the facial muscles, including those of the lips, had yielded evidence of the outstanding position of mankind. Further research should be encouraged. Despite the vast demands of phonetics, linguistics, and psychology, the anatomist should not be deterred from participation in the biological study of the organs of speech. This claim was made in view of a remarkable passage in which Huxley ninety years ago expressed approval of

". . . those who have not made the mistake of attempting to approach biology, either by the high *a priori* road of mere philosophical speculation, or by the mere low *a posteriori* lane offered by the tube of a microscope, but have taken the trouble to become acquainted with well ascertained facts and with their history."

The wise anatomist would treat these words with due respect, but he might recall also Huxley's citation as the last words of his lectures on the morphology of the vertebrate skull in 1864: "*Nil actum reputans si quid superesset agendum.*"

THE MEDICAL WITNESS

PRACTITIONERS AND THE COURTS

A large number of senior students and newly qualified practitioners assembled in the Great Hall of B.M.A. House on Dec. 2 for a lecture, arranged by the Metropolitan Counties Branch, on "The Medical Witness." The lecture was given by Dr. Robert Forbes, secretary of the Medical Defence Union, and the chair was taken by Mr. A. M. A. Moore, later supported by Dr. E. A. Gregg, president of the Branch.

Dr. Forbes said that medical practitioners appeared in courts more frequently than other technical witnesses or members of other professions, and it was conceded by those capable of forming a judgment that in the main they conducted themselves with acceptance and with a consciousness of the important duty they were undertaking. Doctors appeared as ordinary or as expert witnesses. As ordinary witnesses the rules of evidence had to be modified in a certain respect to admit of their testimony, for they were expected to give not only, like other witnesses, their version of the facts but also the inferences to be drawn from them. The expert witness was in a different category. He was not compelled to appear for either side. On being asked to consider the matter, he would indicate what the facts submitted to him signified in his opinion and whether or not his evidence was likely to be of value to the plaintiff or defendant as the case might be. Most doctors considered themselves to be "expert" witnesses in any event, and that in one sense was true, though not according to the legal definition and acceptance of the term. They were, in the main, witnesses to facts, unless they happened to have had special experience or knowledge and to have had no preliminary connexion with the case at issue.

The necessity for keeping records of examination and treatment of patients was emphasized. Incidents regarded as insignificant at the time might come to have a great importance if litigation ensued. Such records were necessary for the protection of the practitioner should he be challenged in a civil or criminal case. Hospital records were often also called for in court, but were not really evidence unless the person who made them was available in court to speak to the notes.

Obedience to Subpoena

The practitioner appearing in a case would usually be asked first to make a report, which would form the proof of evidence. From that moment he should act with the utmost circumspection, making sure that no phrase in that report was such as he could not honestly support in oral evidence. Nothing was more unfortunate during a hearing than that a statement upon which counsel had opened his case should be found at a later stage to require modification. Exaggeration and theorizing—the two rocks upon which many practitioners foundered on their first appearance as medical witnesses—must be avoided. Facts must be defined with exactitude, and the case put no higher than could be substantiated under cross-examination. Partisanship, also, should be eschewed. It was common for a doctor to think that, once employed by a side, he must support their point of view; he should remember that he was there to assist the court to arrive at the facts and that he should leave it to the court to decide the issues. He should try to keep an open mind, always remembering that he might not be aware of all the facts, and that some of his inferences might have to be altered as the case proceeded.

If a subpoena were issued upon a practitioner, and conduct money tendered, and the case were a criminal one, the practitioner was obliged to attend. In a civil action, if a subpoena was served and conduct money not tendered, he was not obliged to attend, but he would be ill advised to refuse. He should indicate to the judge before he was sworn that he had not received conduct money or any fee; this matter should be settled at the outset to avoid subsequent recriminations. It was possible and desirable in a civil action to negotiate with the solicitor in the preliminary stage as to the fees to be paid for current and future services, and to get a letter from him indicating his acceptance of personal responsibility for the payment of the specified fees. At the present moment a B.M.A. Committee was proposing that in civil actions the fee paid to the medical witness for giving evidence on fact only should be 10 guineas for a full day and 7 guineas for a half-day, and for an expert witness that the fee for qualifying—that is, for examining or considering the case so as to give the necessary evidence—should be 10 guineas a day, plus 25 guineas a day for giving evidence.

The history of the tender of conduct money and the payment of a sum for board and lodging was interesting. In days gone by it was laid down that only a "gentleman" was entitled to payment under these heads, and thus it became necessary to define a "gentleman." First the legal authorities admitted that a physician or a surgeon fell within the category of a gentleman; a little later they included a solicitor, and later still a surveyor or architect, and they had not gone much further.

Failure to obey a subpoena might mean imprisonment for contempt of court, and in a civil case it might mean action by a litigant if he could show that he had suffered material damage by the witness's absence or that his case might have been won if the witness had been present. A subpoena should be treated with respect. Possibly on arrival at court the practitioner would find a preceding case still in progress, with many witnesses still to be called, but the heaviest case might collapse suddenly, and the practitioner should not go away without getting definite instructions as to when his case was likely to be heard.

In the Witness-box

Dr. Forbes gave some practical advice on demeanour in the witness-box. The witness should turn slightly towards the judge, and speak clearly and slowly, bearing in mind that the judge was taking notes. He should not resent the humour of some judges nor be intimidated by the formality and severity of others. He should speak so far as possible in non-technical language; after all, he was there virtually as an interpreter. He should not say that the victim was suffering from "contusion of the integuments under the left orbit, with extravasation of blood and ecchymoses in the surrounding cellular tissues, which were in a tumefied state," when in fact he meant that he had a black eye.

Cross-examining counsel in these days were not in the least of the bullying Buzfuz type; there were suave and friendly, possibly inviting the witness to say that he had been qualified for a long time and had had extensive experience, and generally leading him up the garden path. "Don't let cross-examining counsel make you out to be a bigger dog than you are." A proper humility in the witness would impress the judge. It was important not to lose one's temper under cross-

examination, also not to start to argue with counsel. One must beware of the double question and ask that it be divided. The hypothetical question might be encountered: "Now, doctor, if eighteen months ago when you were first called to see this patient you had the knowledge you now have, don't you think you would have done differently?" It was better to be frank and to refuse to theorize on a hypothetical situation. Another piece of advice was that if the witness got the better of counsel he should be careful not to preen himself upon it by nodding to the judge and adopting a "cocky" attitude.

The procedure of endeavouring to agree the evidence with the other side before the case was heard had a great deal to commend it. Sometimes such conferences resulted in settlement out of court. They helped in any event to diminish the likelihood of that unfortunate occurrence whereby one row of doctors said one thing, followed by another row who said exactly the opposite. That left a bad impression, though, of course, on occasion there might be technical issues that were open to doubt, and there were practitioners who must express opposing views about the same case.

Privilege

Finally Dr. Forbes dealt with the debated question of privilege. Not uncommonly a doctor was asked to disclose that his patient had suffered, for example, from syphilis or gonorrhoea. This was not a thing he should voluntarily disclose either to the solicitors or to court, unless, of course, the patient was a consenting party. The privilege vested in the patient, and only the patient could release that privilege. It was open to the medical witness to explain to the judge, before or after he took the oath, that he had been subpoenaed and that he might be asked questions the answer to which would be a breach of professional confidence. He might appeal to the judge to decide whether the questions were admissible. But there was no privilege. A doctor must tell if ordered by the court so to do unless he was prepared to accept imprisonment for contempt of court. Solicitors and barristers enjoyed absolute privilege, but not doctors. The doctor must do what he was told by the judge, but he should do it only after he had made his protest and done all in his power to protect the confidence of his patient.

The speaker concluded by urging the members of his audience when newly qualified to join a reputable medical defence organization to secure assistance in these problems when necessary.

Preparations and Appliances

OXYGEN UNIT FOR NEWBORN INFANTS

Dr. P. C. D. MACCLANCY, assistant paediatrician, Rotunda Hospital, Dublin, writes: The oxygen unit here illustrated (Fig. 1) has been designed as a simple and portable means of providing efficient oxygen therapy for the newborn infant.

The plastic top, 8 by 12 by 10 in. (20 by 30 by 25 cm.), is made from three lengths of 1/4-in. (6-mm.) "perspex" clear sheet, the centre length being heat-moulded to shape. The sides are joined together by plastic screws and rendered gas-tight by a soluble chloroform weld. The curved opening on the distal side, 7½ in. (17.5 cm.) wide by 5½ in. (12.6 cm.) high, is surrounded by five grooved plastic blocks which hold the "collar" of the apron in place. The apron, 42 in. (1.07 m.) long by 24 in. (0.62 m.) wide, is made from plastic curtain material, which is sandwiched between two curved pieces of 1/4-in. perspex sheet 9 in. (22.5 cm.) wide by 6½ in. (15.1 cm.) high. The curved pieces are joined together by plastic screws and the joints rendered gas-tight as above. A 20-c.ft. (0.56-m.³) oxygen cylinder will be found the most convenient size to use, as at the rate necessary to maintain the desired concentration it will last some 8 to 10 hours; further, owing to its relatively small size and weight it is readily portable. The cylinder is fitted with a standard B.O.C. unit comprising pressure-reducing valve, contents gauge, and dry bobbin flowmeter. The oxygen is passed from this to the plastic top via an ordinary Woulfe's bottle.

To provide a concentration of 45–50% oxygen it is necessary to flood the unit at 2 litres of oxygen for two minutes. This concentration can then be maintained by cutting the flow rate down to 1 litre a minute. The carbon dioxide is absorbed by soda lime, some 6 oz. (170 g.) being sufficient for the life of a 20-c.ft. cylinder. The soda lime is put in a wire-mesh container, which is accommodated in a convenient place distant

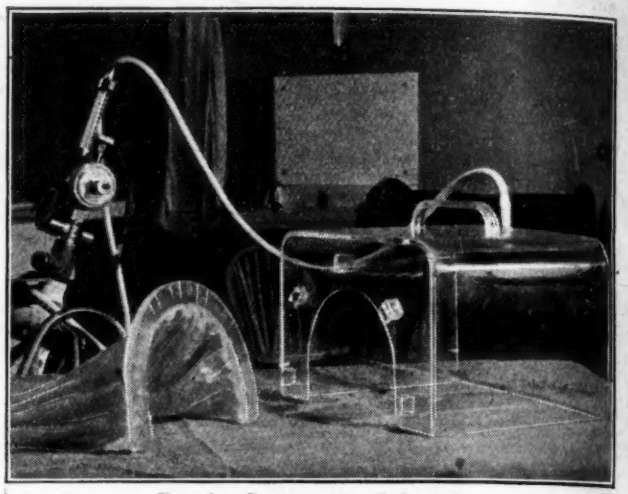


FIG. 1.—Components of the unit.

from the infant's head inside the plastic top. If it is desired, the plastic top can be used alone without the apron; however, if this is done it will be necessary to increase the flow rate to not less than 3 litres a minute to maintain 45–50% oxygen concentration. A rubber hot-water bottle will be found the most convenient means of maintaining the infant's body heat. Heating by electricity is not encouraged unless it can be provided from a closed and spark-proof element. In hospital we use it in the special premature cots so fitted, but here the unit

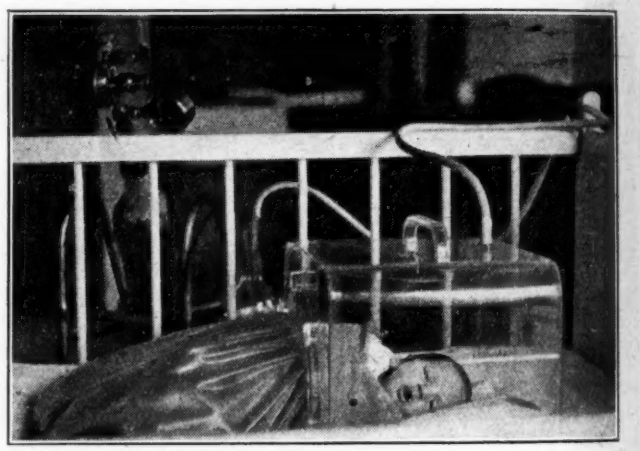


FIG. 2.—The unit in use.

is shown in an ordinary drop-side cot (Fig. 2), a type which is mostly employed in households to-day.

The unit described has given every satisfaction over an extensive trial period in the infants' department of the Rotunda Hospital, and it is intended to have some more constructed, when the plastic top will be "bubble-blown," and consequently devoid of any joinings which may not remain gas-tight in use. It was constructed to my design by Max Models Ltd., Dublin, in conjunction with Medical Gases Ltd., Dublin, who supplied the oxygen fittings.

My thanks are due to Dr. Ninian McI. Falkiner, Master, Rotunda Hospital, and to my senior colleague, Dr. W. R. F. Collis, for permission to publish this description.

Correspondence

Thiouracil in Toxic Goitre

SIR,—While congratulating Dr. Harold Cookson and Dr. F. H. Staines on their meticulous and unbiased record (Nov. 15, p. 759) of their four years' experience of the use of thiouracil in toxic goitre, we wonder whether they have really provided evidence for their claim that "there is no doubt that the antithyroid drugs now available have established themselves as a most valuable addition to the methods of treatment of toxic goitre, and in certain types as the method of choice." It would, indeed, appear to us that their experience constitutes the most devastating indictment of the use of these drugs in treatment that we have yet read. We do not for a moment question their findings, for they are in line with those of many other observers both in America and in Great Britain, but we do question their conclusions.

The facts appear to be as follows: (1) 95 patients were treated. (2) In 6 no control was obtained. (3) Remission of the disease lasting from 2 to 25 months was obtained in only 40 patients; 15 of these had relapsed. (4) 14 patients suffered from toxic effects of the drug with its abandonment on this account in 2 cases and with one death from agranulocytosis. (5) *No fewer than 10 patients died while under treatment.* Items (3) and (4) in this list contain sufficiently formidable implications of wasted time and effort on the part of both doctors and patients. But it is a mortality, while under treatment, of over 10% that constitutes the most damning evidence of all.

Although 8 of their patients had to be submitted to surgery without a fatality, the writers of the article do not permit themselves any general comparison between their results and those of surgery. They can scarcely be unaware, however, since it has been stated on many occasions, that subtotal thyroidectomy, given good surgery and good management both pre- and post-operative, can be performed on hundreds of consecutive patients with a mortality of less than 1%. These series include patients of all ages and with every degree of severity of the disease (none are rejected), and it is recognized with gratitude that thiouracil is of the greatest service in the preparation of severely toxic patients for surgery.

Dr. Cookson and Dr. Staines have treated 16 patients who had reached the stage of auricular fibrillation. In only half of these was a normal rhythm restored with thiouracil, and 4 died while under treatment. Surgery, on the other hand, claims many of its most brilliant results from among this very seriously ill group of patients, and with the occasional help of quinidine less than 20% fail to obtain a persistently normal rhythm.

In view of these well-established claims we do not understand how the writers of this article can conclude that thiouracil can be the best method of treatment in any type of the disease. It may be argued that the best surgery is not available for more than a fraction of the sufferers from thyrotoxicosis. If this be so, our answer is that opportunity is available for any surgeon to learn the technique and management of the operation. There is no excuse at this date for the plea of ignorance, and it would be bad surgery indeed that resulted in the loss of over 10% of its patients.—We are, etc.,

GEOFFREY KEYNES.
J. W. LINNELL.

London, W.1.

Diet and the Nation's Health

SIR,—No cautious man would willingly descend into the dusty arena where the gladiators contend about the state of the nation's nutrition, and I formally disavow any expression of opinion on the subject here. I am moved to commentary, however, by the account in your pages (Nov. 29, p. 882) of a recent debate of the Hunterian Society. Sir Jack Drummond, it would seem, expressed the view that there is "no objective evidence showing with clarity and precision" that we are less well nourished than in 1938, and implied that he is not prepared to accept "merely subjective impressions" in a contrary sense.

His antithesis, suited perhaps to the occasion, is resounding rather than substantial, yet he may be right in the first part of his statement. But surely to assume that in so saying he has disposed of the problem under discussion is to beg the question and to display a misunderstanding of the nature of the problems facing the clinician, the obligations laid upon him, and the means by which he has to deal with both. "Subjective" impressions, and with all respect to Sir Jack Drummond I confess that I know of no other kind, are surely the beginning, if not the end, of that observational approach from which all scientific inquiry must start—an approach, too, that must remain the clinician's principal one.

Every clinician yearns for nature to provide him with "objective data showing with clarity and precision" what is wrong with his patient, and desires whenever possible to measure, verify, and control his observations and to confirm his preliminary impressions. But he knows that too often this is not the order in which things happen in the practice of medicine, that he is constantly being forced to pay careful attention to his subjective impressions and to lay and initiate plans of action in the interests of his patients long before clarity and precision of data are vouchsafed him. If he is not willing to go to work in this way, then he is incompetent to discharge his obligations and were better employed conducting nutritional experiments on rats in a laboratory. There, at any rate, he could afford to wait for clarity and precision, to let time do his thinking for him, and to see his animals visibly pining before he was under the painful necessity of making up his mind. How wonderful it would be did such easy options govern the labours of the physician, who would then rarely be compelled to call upon intuition or to use judgment but could sit back waiting for complete data to drop into his lap.

I suggest, therefore, that where the health of human beings is in question scornfully to reject subjective impressions as part of the material of judgment, and to decline to cerebrate in the absence of data of complete clarity and precision, would be as unscientific and negligent as to suppose that subjective impressions are of themselves wholly adequate as evidence and absolve us from the obligation of all further inquiry. In the present instance, perhaps, it is of little importance what the physician thinks or says, since he has no control over what the nation gets to eat; but that one who has been a scientific adviser to the Ministry of Food should take the narrow view of evidence reflected in Sir Jack Drummond's remarks is more serious. He may be right in thinking that the nation is not undernourished, but his criteria of assessment are inadequate to a situation which he appears not to understand.

The biochemist, indeed, has proved notably insensitive to intimations reaching him from medicine, and our bones might easily rattle under our hides before his convention of scientific purism permitted him to see that we were growing empty. If one were at all cynical, one might be tempted to hope that this nation may never be so very hungry that the biochemist comes to notice the fact.—I am, etc.,

London, W.1. F. M. R. WALSHE.

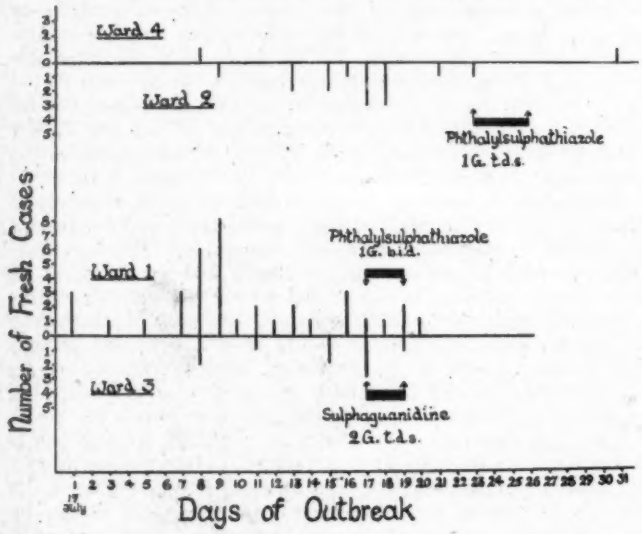
Acute Non-specific Gastro-enteritis

SIR,—In view of the increasing attention directed to outbreaks of gastro-enteritis of unknown aetiology, a description of an outbreak in this mental hospital last summer may be of interest. The first case began on June 9, the outbreak proper on July 17, and thereafter fresh cases appeared for 30 days, involving 65 out of 309 patients.

The outbreak began in an infirmary ward, where, contrary to the experience of Cook and Marmion,[1] it involved 41% of the patients, principally the old and feeble and those debilitated by other diseases. Eight days later cases appeared in two other wards, the day after that in a fourth, the whole of the female block now being affected. Cases of gastro-enteritis were present in the district, but in the hospital were limited entirely to the female wards. Two female part-time nurses developed it; one had had no direct contact with the affected wards, the other had been nursing there. Some members of the male staff living at home contracted it, but did not infect any of their patients. As in other outbreaks, food as a source could be excluded, as both male and female patients ate from a common kitchen. There was no association with Sonne dysentery,[2] upper respiratory infections[3] or chilling.[4]

Clinically the onset was abrupt, with diarrhoea, vomiting, and griping abdominal pain; it was apyrexial except in 3 cases, where the temperature rose 1°–2° F. (0.6°–1.1° C.) to subside in 24 hours.

The vomiting ceased within 24 or at the most 48 hours, while the diarrhoea, which was of frequent, offensive, watery stools without blood or mucus, lasted two to three days, exceptionally four or more. In a few the onset was severe with marked prostration. One-fifth of the cases had no vomiting. Each case had a minimum of 3 stool cultures, 201 specimens in all being examined. No organism of the enteric, dysentery, or salmonella groups was found except in one case. This patient's illness lasted longer than usual—namely, 7 days. On the first, fourth, and eighteenth days from the onset her stool was negative; on the twenty-fourth day *Salm. typhimurium* was isolated. She was the only patient to have a further attack (not shown in these figures), which occurred two months after



the first, when her stools were again negative. Widal tests from this patient and 6 others on Sept. 17 were negative. The following organisms were also identified, the numbers in brackets referring to cases: Morgan's bacillus 1 (4), Morgan's bacillus 2 (1), paracolon-bacillus type (4), *B. faecalis alkaligenes* (1).

All cases were immediately isolated, discovery frequently depending entirely on the nurses' observation. In all but the infirmary ward strict isolation of individual patients could be enforced. Treatment was on the usual lines, with initial starvation and gradual return to normal of the diet by the fourth or fifth day. Attempts to increase the diet more quickly led to recurrence of the diarrhoea. Some cases were given phthalylsulphathiazole 3 g. daily without marked effect on symptoms or duration. However, sulphaguanidine and phthalylsulphathiazole were tried as prophylactics, as shown in the table and diagram. The results were encouraging.

Ward	Population	Type	No. of Cases	Duration	Prophylaxis	% Affected
1	90	Infirmary; aged and sick; overcrowded	37	July 17–Aug. 5	Phthalylsulphathiazole, 1 g. b.i.d. for 2 days	41
2	88	Refractory overcrowded	15	July 25–Aug. 8	Phthalylsulphathiazole, 1 g. t.d.s. for 3 days	17
3	98	Overcrowded; patients out to work	10	July 24–Aug. 4	Sulphaguanidine, 2 g. t.d.s. for 2 days	10·2
4	33	Parole; not overcrowded	2	July 24–Aug. 16	None	6

When sulphaguanidine was given to all patients in Ward 3 the incidence of fresh cases stopped abruptly; one case appeared on the second day of prophylaxis, but her symptoms were mild and lasted only 24 hours. In Ward 1 phthalylsulphathiazole could be given to only a proportion of patients owing to low stocks. Two cases occurred on the second day of treatment and one the day following, all in patients who had been given the drug. Probably the dosage was too small. Fresh cases continued to occur in Ward 2 until phthalylsulphathiazole in a somewhat higher dosage was given to all patients.

An interesting point is that in Ward 4, where no measures beyond isolation of the patients affected were taken, only two developed gastro-enteritis. Here there was no overcrowding and the patients were out most of the day. In Wards 1 and 2 there was close all-day contact between patients, and in Ward 3 close contact all night and part of the day.

The course of the outbreak suggests that the initial cases were caused by one or more carriers from outside and that infection thereafter spread directly from case to case, probably air-borne. Social functions were in abeyance, and so there was no contact between male and female patients. The sulphonamides appear to have a definite prophylactic value, but further trial would be necessary before a positive statement could be made. Similar claims were made for mepacrine[5] which have not been borne out.[1] Even allowing their value, the incidence was directly related to the degree of overcrowding. The exceptionally high incidence in the infirmary ward may be explained by the difficulty of completely isolating so many, of "spotting" early cases among the totally demented by an already overworked nursing staff, and of controlling the excretions of the faecal incontinents.

The clinical course of the illness suggested a rapid invasion with most of the damage at the outset, which may explain why the sulphonamides were effective in prophylaxis but not in treatment.—I am, etc.,

Bracebridge Heath Hospital, nr. Lincoln. WILLIAM FORSTER.

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2 Martin, L., and Wilson, M. M. (1947). *Lancet*, 1, 553.
3 MacGregor, I. (1946). *British Medical Journal*, 2, 225.
4 Kershaw, G. R. (1947). Ibid., 1, 717.
5 Freedman, B. J. (1946). Ibid., 2, 552.

"Q" Fever

SIR,—I was more than interested in the article on "Q" fever by Drs. J. E. Caughey and J. A. Dudgeon (Nov. 1, p. 694). Well do I remember reading the article in question on "Primary Atypical Pneumonia" which has turned out to be an epidemic of "Q" fever. The lesson to be learned from this is of prime importance in my opinion. To my mind it is a great pity that the term primary atypical pneumonia was ever introduced, because at the best it is vague, confusing, apt to be misleading, and falls readily from the lips of those who are satisfied with a diagnosis which usually depends on so-called typical radiological appearances in the lungs or, in their absence, on so-called typical findings on auscultation of the chest together with the general symptoms of a febrile virus infection, a white count usually below 10,000 per c.mm., and the occasional presence of a rash, splenomegaly, lymphadenopathy, etc. The presence of cold agglutinins in the serum is said to place the diagnosis beyond all shadow of doubt, but greatest stress is usually laid on the radiological findings and the physical signs in the chest.

Physicians who have much experience of febrile diseases, especially prolonged febrile illness in tropical and subtropical countries, realize how often there are present abnormal signs on auscultation of the chest, but these as well as positive radiological findings in the lungs do not necessarily result in a diagnosis of pneumonia of some sort—e.g., primary atypical pneumonia, "pneumonia," or "pneumonitis." Such cases, with or without evidence of radiological findings in the lungs and with a white-blood count of less than 10,000–12,000 per c.mm., are invariably investigated along the lines of a case of P.U.O., which includes blood films and thick drops for malarial parasites, blood cultures, repeated total and differential white-blood counts, appropriate agglutination reactions when facilities are available, and the other relevant investigations. I wonder how many cases of enteric-group fever, other septicaemias, and typhus-group fever, etc., have been diagnosed as primary atypical pneumonia or just "pneumonia."

I never make a diagnosis of primary atypical pneumonia until the last resort, as I believe that such a diagnosis should not be made until all relevant investigations have been carried out and all other relevant causes have been excluded. In this way errors in diagnosis should be lessened. Too often are certain febrile diseases excluded on the degree of the severity of the signs and symptoms or on the absence of some so-called typical sign or symptom. The converse is also true. This attitude is indicative perhaps of book knowledge and is characteristic of self-confidence in the inexperienced. Not infrequently I have seen physicians on clinical grounds alone exclude, with what appeared to be confidence and to their own satisfaction, such diseases as enteric-group fever, typhus-group fever, leishmaniasis, hepatic amoebiasis, and even plague, while later laboratory evidence revealed the true nature of the diagnosis. Surely it is about time that it was universally appreciated that specialist investigations are not just carried out to confirm a clinical diagnosis. Happily that day is at least passing—although not quickly enough—because so often such specialist investigations are necessary to make the diagnosis. Unfortunately some young physicians go to the opposite extreme

and carry out all sorts of specialist investigations before taking an adequate history or making a thorough clinical examination. No doubt the pendulum will settle. The ability to think of likely and not unlikely causes of an illness and their adequate exclusion is what is wanted and not just the ability to repeat verbatim textbook description of disease—a not uncommon failing.

What is pneumonia and what is primary atypical pneumonia? Surely there are different causes of pneumonia, some of which are known—e.g.: (1) Bacterial pneumonia, which may be due to pneumococci, staphylococci, streptococci, *B. tuberculosis*, *B. typhosus*, and *B. pestis*, etc. These are further differentiated by their sensitivity or otherwise to penicillin and/or sulphathiazole, etc. (2) Virus pneumonia due to known and unknown viruses—e.g., influenzal pneumonia, psittacosis, so-called primary atypical pneumonia, etc. (3) Malarial pneumonia, pulmonary amoebiasis, pneumonia due to ascariasis and relapsing fever. (4) Pulmonary manifestations of yeasts and fungi. (5) So-called rheumatic pneumonia. (6) Lipoid pneumonia, and no doubt other causes of pulmonary pathology apt to be diagnosed as pneumonia or pneumonitis.

Each infecting agent may produce a typical or atypical picture, so why label one type of infection believed to be due to a virus as primary atypical pneumonia? Why not call it just a virus pneumonia, or, in the present state of our knowledge, why not just describe it as a case of P.U.O.? In cases so labelled exhaustive investigations are invariably carried out. Accordingly I would suggest that febrile illnesses of indeterminate origin should not be given what appears to be a definite diagnosis as "primary atypical pneumonia" would appear to be, otherwise encouragement would be given to the use of the term in cases of febrile illnesses with abnormal signs in the chest the origin of which is not known, vague, or uncertain. Well do I realize that many physicians to-day regard signs in the chest in a febrile illness of doubtful origin merely as a pulmonary manifestation of a generalized disease process and search assiduously for the cause. For them, as well as for those who leap to a diagnosis of "pneumonia" and to the rapid exhibition of penicillin and/or sulphathiazole, the paper of Caughey and Dudgeon should be invaluable.—I am, etc.,

B.A.O.R. JOHN MACKAY-DICK.

BAL and Malnutrition of the Nervous System

SIR,—Dr. W. Russell Brain in his most valuable contribution (Nov. 15, p. 763) referred to Peters's work on BAL. May I state this had also caught my interest. Among those who gave so much help in West Africa one must mention the name of A. Clark. The writer met him on his arrival there and owes much to his guidance. It marked also a friendship which lasted till his death in New Zealand early this year. At that time I had come to the conclusion that the food cause of nutritional retrobulbar neuritis, with its associated conditions, was due to manioc ("gari").

In the therapeutic field naturally one was wholly dependent on knowledge gained from the biochemist. Neither nicotinic acid nor riboflavin had then been discovered. Clark was a biochemist, and his views greatly impressed me, for he advanced the theory that manioc, like sugar-cane in the West Indies (where H. H. Scott had described an identical syndrome, though of a more fulminating type), contained a cyanic glucoside, and this inhibited sulphur utilization by combining with it to form a thiocyanate and so prevent acute poisoning; but if the intake of protein itself was insufficient, then this condition was precipitated. I must add, however, for a number of reasons affecting one's later inquiries, I do not consider Clark's theory can be directly maintained.

I carried out a number of therapeutic trials with various sulphur derivatives, including intravenous sodium thiosulphate, but I found personally they all failed to influence the condition (see *W. Afr. med. J.*, 1937, **9**, 35). But this is not a reason, for it was appreciated one was not really using an assimilable sulphur. Following extensive inquiries in other parts of the world, it had become clear that neither manioc nor sugar-cane could be wholly incriminated, as the syndrome could recur independently of either. Thus the Malayan dietary at Changi (where Landor and Pallister demonstrated this condition in 1935) showed the staple carbohydrate was rice. Again we know now, of course, part of the syndrome at least was due to an ariboflavinosis, though how much the neural lesions are due to that is problematical. So far as a food cause could be identified we had not advanced very materially from the old "Deeks theory" of excess carbohydrate-diminished protein intake, though one feels it is reasonable to add it had become possible to show that only certain carbohydrate sources of a specified type appeared more directly involved—cf. manioc, sugar-cane, and "English" rice. Also there was no doubt of the protective value of certain protein foods.

In the therapeutic field by 1938 (Moore, *J. trop. Med. Hyg.*, 1939, **42**, 109) it had also become possible to show autoclaved "marmite" (excluding vitamin B_1) cured the *earlier* case of nutritional retrobulbar neuritis just as formerly it had been shown to respond to ordinary marmite. Nicotinic acid had no appreciable effect. But I have always felt Clark had touched on part of the truth, and it is possible that, under conditions of dietaries already referred to, sulphur metabolism may be disturbed. I am not qualified to express any views as a biochemist, and one's own investigations have always been centred on clinical, therapeutic, and dietary survey of these cases. It seems also to the writer it is more than coincidental that arsenic can bear some comparative clinical relationship with these deficiency syndromes. Therefore it might repay us to test Clark's work further, and this supposition, by the use of BAL, which has been only recently discovered. It might prove of interest also to try BAL on swayback. Clark was extremely familiar with this animal-deficiency disease in New Zealand and referred to it in his arguments. (Here again he maintained the cause was a cyanic glucoside in the white clover, and he viewed cobalt as protective.)

Clark's work is published mainly in the *Trans. roy. Soc. trop. Med. Hyg.*, 1932, **26**, 301; *Certain Aspects of Poisoning by Food Plants in Nigeria, 1934–6*; *J. trop. Med. Hyg.*, 1936, **39**, 269; and from 1936 onwards in a series of articles in the *J. trop. Med. Hyg.* Admittedly the suggestion for therapeutic trial with BAL is conjectural, but to the writer it does seem worth while to explore in active cases, so far as is possible, every avenue which may present itself, provided we do not risk delay in effective treatment,—I am, etc.,

Cheltenham. D. FITZGERALD MOORE.

Battle Neurosis Treated with Leucotomy

SIR,—The article by Drs. William Sargant and C. M. Stewart (Nov. 29, p. 866) raises some interesting and perhaps controversial issues. There is no mention or speculation in the report as to the factors underlying the emotional conflict which manifested itself in neurotic symptoms. This does not, of course, mean that the psychodynamic viewpoint was not considered, but may it not be the absence of any discussion on this basis that tends to cause uneasiness among psychiatrists at reports of the more radical physical treatment of the psychoneuroses? This is not to say that there is no justification of the treatment of any particular case by such methods as electric convulsion therapy and leucotomy. Indeed, facilities for the treatment of chronic psychoneurosis are nowadays so limited that any method which produces results has to be considered. Nevertheless, as long as psychoneurosis is conceded to be the result of emotional conflict, are we not entitled to know or at least to inquire what are the pertinent factors in such cases?

In the case reported the pre-morbid personality gives indications of obsessional traits and might be designated an obsessional character. That the patient had a high morale is suggested by his leaving a safe civilian job for a highly combatant one for which events proved he was ill-suited and which led to increasing tension and finally breakdown. One may speculate as to the subsequent history of this case had the war ended in November, 1944, at which time a slight wound had given him an honourable exit from battle. The real conflict which led to a persistence of his symptoms after that time may well have arisen from the feeling of failure in the high task which he had set himself. Intense guilt feelings may have been aroused from which the personality appears to have struggled wildly to escape by paranoid, hysterical, hypochondriacal, and depressive reactions.

"He always seemed unable to gain insight into his symptoms" might surely have been interpreted that the personality could not tolerate this insight, and in this lay no doubt the lack of success with abreactive and exploratory methods and the amelioration of the condition by sedation. Whether a more gradual and long-term psychotherapeutic approach such as psycho-analysis would have produced a better result is a matter for speculation. This might at least have succeeded in modifying the superego and enabled the personality of the whole to suffer less from feelings of guilt.

Might one not speculate as to whether prefrontal leucotomy does much the same thing as this but at some cost, not properly known at the present time, to the personality as a whole?

From a limited experience of the operation the impression is gaining ground that the presence of pre-morbid obsessional traits is of good prognostic significance when considering candidates for leucotomy. This appears not only to explain the good results claimed in obsessional neurosis and depression but appears to be at the back of the improvement obtained in this case. Before accepting the operation as the treatment of choice in any case of psychoneurosis a thorough exploration and evaluation of the psychodynamic factors are indicated, and only if these are considered unmodifiable by any other practicable means should the operation be recommended.—I am, etc.,

Shenley, Herts. B. C. GILSENAN.

SIR,—I was glad to see the article by Drs. William Sargant and C. M. Stewart (Nov. 29, p. 866) reporting a case of such battle neurosis treated by leucotomy. Sincere clinical reports, however inadequate they may be from the psychologist's viewpoint, are much needed. In the final comment it is said that the case is reported partly to encourage patients and relations to agree to this form of treatment when it is recommended. It must be agreed that in the matter of leucotomy the final decision must come from the good sense of the lay public, doctors being perhaps less able than other people are to see wider issues than the immediate relief of an individual's symptoms and distress.

There is still one doctor, however, who hopes that the public that clamours for whatever is on tap at the moment will stop short of asking to be leucotomized. He has lost hope that those who in their distress cry out even for a mutilating operation may be refused what they ask by the doctors themselves.—He is, etc.,

London, W.1. D. W. WINNICOTT.

The Waning Power of Penicillin

SIR,—It is suggested that penicillin-resistant strains of bacteria are largely bred by the indiscriminate prescribing of penicillin ointment for such conditions as styes, acne, etc. The general practitioner cannot test organisms for sensitivity, but I am sure that many of us would be unwilling to surrender such a valuable method of treatment.

In my limited experience, all cases of breast abscess, carbuncle, and multiple furunculosis that have been treated with an initial exhibition of 500,000 units and four of 200,000 units at twelve-hourly intervals have undergone complete resolution. I have had some failures, such as cases of cystitis, treated with the same dosage, but as the organisms were probably not sensitive to penicillin I do not consider a clinical trial was bad medical practice or likely to breed resistant strains. Perhaps if local applications were withdrawn from the market and a minimum dosage advised, the potency of this valuable drug might be safeguarded.—I am, etc.,

Fareham, Hants. G. G. THYNE.

Allergy to Penicillin

SIR,—The article by Drs. A. G. Wilkinson and K. Zinnemann on allergy to penicillin (Nov. 29, p. 865) prompts me to make a few observations on this subject. The severity of reaction in the case described is not an uncommon occurrence, although milder forms are rather more frequent. However, it should be realized that all degrees of severity can be seen from the mildest in the form of a localized patch of urticaria at the site of injection to the severe type of serum-sickness-like syndrome with generalized urticarial dermatitis, angioneurotic oedema, and involvement of the visceral organs. The attention of clinicians should be drawn to two other types of reaction to parenteral penicillin : (*a*) immediate febrile reaction, (*b*) scarlatiniform erythema with constitutional symptoms. Finally, an acute arteritis with thrombosis has been reported in France by Courty and Biscaye *(Presse méd.*, 1947, **64**, 734) as a complication of penicillin hypersensitivity.

Recent experience has taught me that allergic reactions are not more frequently met with in subjects who had received penicillin previously. Of 20 personal cases, seen in the year 1947, three only gave a history of previous penicillin administration. One of these, a woman of 47, developed in April, 1946, a penicillin-sensitization eczema on the left leg following local use of penicillin cream. A year later parenteral penicillin for an eye infection produced a severe allergic reaction comprising pruritus, vomiting, malaise, and giant urticaria of a very protracted nature. It was interesting to note that the skin lesions first appeared on the same left leg at the site of the one-year-old scar.

The more I see of allergic manifestations to parenteral penicillin the more I am inclined to believe that they are due to the impurities contained in the commercial batches. French observers are of the same opinion. So far I have not seen allergic accidents follow the exhibition of the white crystalline penicillin nor have I seen any reported in the literature. Thus, if a reaction occurs during penicillin administration, my practice is to stop immediately the offending penicillin and finish the course of treatment with crystalline penicillin. The crystalline preparation would also be indicated in all subjects known to be allergic to the ordinary yellow variety.

Mild reactions do not present a therapeutic problem. "Benadryl" is useful, and other antihistamine drugs may be tried—for instance, "antistin" given orally produced dramatic improvement in a severe case of penicillin-allergic reaction resistant to all other forms of treatment. New and more powerful antihistamine substances are becoming available—such as Halpern's 3277RP—and it is hoped that the problem of symptomatic treatment of allergic manifestations will be satisfactorily resolved in the near future.—I am, etc.,

London, W.10. A. I. SUCHETT-KAYE.

SIR,—I have read the article by Drs. A. G. Wilkinson and K. Zinnemann (Nov. 29, p. 865) and would like to report that I have had two similar cases following penicillin treatment. Both occurred in women about 8–14 days after treatment, and the symptoms were similar to a severe serum reaction with swelling of the joints. The response to treatment with antihistamine drugs was poor, and there was a relapse in both cases after a few days.—I am, etc.,

Coventry. S. NATHAN.

Pregnancy after Lumbo-dorsal Sympathectomy

SIR,—In the annotation on the above subject (Nov. 29, p. 876) you suggest that there is need for further knowledge of the effect of this operation on uterine action in labour. Observations were made by Todd during 1936–8 on eight of my cases who for various reasons had had extensive bilateral lumbar sympathectomies.

The number is small, but the observations were exact because Todd with admirable keenness succeeded in being present at each labour. He told me that he had not noted any deviation from normal in any one of the eight. Todd's observations would no doubt have been published at length had not the life of this most gifted gynaecologist been cut short in France in the early days of the war.—I am, etc.,

Prestatyn, Flintshire. E. D. TELFORD.

Relief of Pain in Pelvic Cancer

SIR,—The statement in the annotation on the above subject (Nov. 29, p. 875) that "the operation of pre-sacral neurectomy has no significant ill effects" should not be allowed to pass unchallenged. Learmonth was the first to point out that the pre-sacral nerve contained motor fibres for the musculature of the seminal vesicles, ejaculatory ducts, and prostate gland. In at least one reported case the patient, a male, became sterile after the operation. It is most unlikely that this complication will cause medico-legal difficulties in patients with pelvic cancer, but the operation is performed for other diseases, and the full physiological results should be known.—I am, etc.,

London, W.1. J. H. CARVER.

Reiter's Syndrome and Abacterial Pyuria

SIR,—Baines[1] in a recent article quoted me as having strongly pressed the role of *Trichomonas vaginalis* in abacterial pyuria, but I am at a loss to discover how the reference[2] could have led him to this erroneous conclusion, since I pointed out that one of the chief diagnostic features of T.V. urethritis is the presence in the smear of "large numbers of mixed organisms," which, by definition, excludes abacterial pyuria. In the syndromes under discussion I am therefore in complete

agreement with Mr. Baines in dismissing as causative factors *Trichomonas vaginalis* infection with that of gonorrhoea and dysentery. I find, however, his conclusion that Reiter's disease and abacterial pyuria are variations on the same aetiological theme and that they are always "venereal" in nature much more difficult to accept. May I give as briefly as possible the main results from a fairly considerable experience with cases of this nature which passed through my department during service in the Middle East?

In 1941–2 the early cases of Reiter's disease admitted to my department were missed, since self-administration of sulphonamides was so common before reporting that smears and cultures, negative for the gonococcus, in cases of urethritis, arthritis, and conjunctivitis were suspect and certainly not sufficient to suggest the discovery of a new disease. Two cases, however, occurred which convinced me (and I was difficult to convince) that here indeed was a syndrome without a venereal history in *some cases*. From that time cases presenting this triad were investigated not only in my department but in the associated dysentery and ophthalmic sections of the hospital with the following results:

(1) The conjunctivitis may precede the urethritis in some cases. (2) The conjunctivitis may be so mild that only a very slight injection of the conjunctival vessels is present. In this connexion it was found that slit-lamp examination revealed tiny bead-like lesions deep in the lower limbus of the cornea which on clearing left minute striae. One case, presenting urethritis and arthritis but who gave a history of conjunctivitis a few weeks previously, showed these tell-tale scars, and it is suggested that this sign is looked for in future cases. Perhaps conjunctivitis indicating inflammation of the conjunctiva is not therefore a true description of the "red eye" in Reiter's disease. (3) Prolonged search among literally hundreds of cases of dysentery in the hospital failed to reveal a true case of the syndrome. (4) Treatment had no effect on any of the triad. Recovery was the rule, but was often delayed for a period of months. (5) Scanty Gram-positive diplococci were found on a few occasions, but cultures were negative. In most cases no organisms were found. (6) The complete success with arsenic in abacterial pyuria in my opinion placed this syndrome in its own category and suggests that the infecting organism will be found to be as highly organized at least as the spirillum, from our knowledge of the therapeutic effects of arsenic in other infections.

Finally, although clinical impression can only be subsidiary as evidence, I came to the conclusion (*a*) that virus infection of "swimming-bath conjunctivitis" and virus cervicitis in the female were both possible sources of infection in cases of Reiter's disease; (*b*) that usually it is a systemic infection with local signs dependent on local tissue peculiarities. And in this connexion I have made a tentative suggestion, as yet unpublished, of yet another factor which may play a part not only in cases of this nature but also in the systemic complications of gonorrhoeal infection.—I am etc.,

London, W.1. F. L. LYDON.

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2 Lydon, F. L. (1945). Ibid., **2**, 384.

Unusual Pregnancy

SIR,—The following case may be of interest to you.

CASE REPORT

A girl, a primipara aged 27, consulted us in early January of this year complaining that she was losing blood per vaginam. On examination it was found that she was three months pregnant, the last menstrual period being on Nov. 17, 1946. The uterus could be felt just about level with the pubis; the cervix was soft, and she was losing blood. She was put to bed and given 5 mg. of "lutocyclin." Four days later she aborted a foetus, complete in its sac, about 1/2 in. (1.25 cm.) long. She was kept in bed for a further six days, and, her lochia having dried up completely, she was allowed to get up. Three days later she was called away urgently to nurse her mother with pneumonia, and on her return six weeks later she came to see me for a post-natal examination. She had been very well during the time she had been away, had done a lot of heavy work, and was feeling very fit.

I was somewhat surprised to find the uterus up to the umbilicus, and her Ascheim–Zondek test was positive, so I hastily rebooked her for her maternity care and proceeded with a routine antenatal examination.

On July 25 she was delivered with ease of a 5½-lb. (2.5-kg.) male child, and ten minutes later the placenta appeared at the vaginal orifice. No further detachment took place, and after two hours her condition began to deteriorate. She was given a general anaesthetic, and on manual examination it was found that about three-quarters of the placenta was in the vagina. The uterus was contracted down hard, and under very deep anaesthesia further relaxation was obtained to get the hand into the body, and it was found that there was a thick fibrous adhesion (1/2 in. thick) between the placenta and the uterine wall on the right-hand side of the vault. This was with difficulty divided and the placenta was delivered. The girl's puerperium was uneventful.

It would appear that this girl aborted one foetus during pregnancy and successfully carried the second baby to within a fortnight of her term. At the side of the first foetal implantation adhesion occurred between the remaining child's placenta and the uterine wall, possibly in a clot left by the abortion of the first foetus. In view of the fact that the second child went almost to term, one cannot suppose that this is a case of superfecundation. Neither my partner nor I have personally seen this sequence of events before, but it would appear to have followed a logical course.—I am, etc.,

Ruskington, Lincs. T. SMALLHORN.

Retained Placenta

SIR,—A woman who had just been delivered of her second child in spite of having good uterine contractions every 3–4 minutes was still undelivered of her placenta at the end of 35 minutes. There had been no bleeding. She was then placed in the squatting position over a bedpan, and the placenta was delivered with the next contraction—coincidence, perhaps, but worth trying as the first measure in all patients who are well enough to co-operate.—I am, etc.,

Winfrith, Dorset. P. R. BOUCHER.

Myocarditis of Pregnancy

SIR,—I had recently what appears to me to be a case which would be interesting for publication. The following briefly are the facts of the case.

CASE RECORD

A married woman aged 34 years was admitted to the County Hospital, Roscommon, on Oct. 11, 1947, having a history of three months' pregnancy, but bleeding on and off for a week prior to admission to hospital. On examination after admission she had a fairly heavy dirty vaginal discharge. She was thin and pale in appearance and she said she did not feel well. P.V. on admission: The os was sufficiently dilated to admit one finger. The uterus was about 2–3 months in size and was soft and flabby. On the examining finger was a mixture of thick pus and blood. A culture of this material produced a predominant *Staphylococcus aureus*.

She had no pyrexia. Her pulse, however, was very irregular. At the wrist there were two beats occurring regularly together within a very short space of each other. After these there was an evenly spaced two beats, more like normal heart beats, and again after these the two beats occurring quickly together. The pulse went on in this regular irregular fashion. At the apex the heart beats were of the same pattern as the beats at the wrist—namely, two normal heart sounds, a long pause, then two beats occurring quickly together, with a long pause and again two normal beats.

An electrocardiogram taken on Oct. 13, of which I enclose lead III (Fig. 1), shows what I take to be two ventricular extrasystoles occurring regularly together, interspaced between two normal PQRS complexes. The other leads (I and II) showed similar abnormality.

It was decided not to interfere with the uterine condition but to treat her conservatively. She gradually improved, her discharge ceased, and it was noted on Oct. 23 that her pulse was of normal rhythm. I took a cardiogram on Oct. 24—that is, twelve days after admission; I enclose lead III of this cardiogram (Fig. 2). It shows the heart beating regularly and normally without any ectopic beats. Leads I and II were also normal. She felt well and was discharged home on Oct. 26.

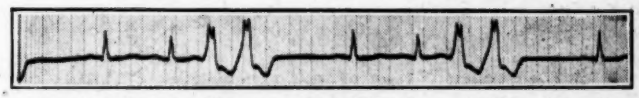

FIG. 1.—Electrocardiogram (lead III) taken on Oct. 13, 1947.

FIG. 2.—Electrocardiogram (lead III) taken on Oct. 24, 1947.

These, Sir, are briefly the findings in this case, and I consider it rare and interesting for the following reasons. (1) The heart condition seems to have been a toxic myocarditis causing ectopic ventricular beats. (2) The toxaemia was mild, causing no temperature or tachycardia. (3) In my library I cannot find any cardiograms like the tracings found in this case. (4) The clinically alarming condition of her heart and the rapidity with which it cleared up.—I am, etc.,

Roscommon, Eire. JOHN J. WALLS.

Obstetric Emergency Service

SIR,—Mr. Frank Stabler's excellent paper on the Newcastle-upon-Tyne obstetric emergency service (Nov. 29, p. 878) gives me an opportunity to make a point of which I became convinced as an obstetric H.S. and the value of which I have since had a chance to confirm in general practice. This is that the general practitioner's obstetric bag should include either saline or plasma and a giving set. If he is to be called by the midwife in emergency he should at least bring these simple requirements; in this way he may very well save some of those cases which the "flying squad" admittedly cannot reach in time. He can put up a drip before undertaking manual removal of the placenta—a precaution which I find gives considerably increased confidence. Should the flying squad be called they arrive to find the transfusion arrangements ready set up and can the more quickly continue with any obstetric manipulations that may be necessary.

I would suggest that the regional transfusion officers might organize the supply and turnover of saline and standard giving sets to practitioners. After all, since the war there must be very few practitioners under the age of 50 unfamiliar with simple transfusion apparatus. The supply of plasma might, however, be impracticable. Such apparatus will also come in useful in pit accidents, and its availability on the spot has saved the life of one of my fellow practitioner's patients in this area.—I am, etc.,

Morpeth, Northumberland. R. P. ROBERTSON.

SIR,—If penicillin resistance is to raise its hydra head, manual removal of placenta may well regain pride of place as the most dangerous operation in midwifery. One pictures the modern scene. By the time Mr. F. Stabler has scrubbed up and donned a pair of dry sterile gloves (another pair, of the right size, lying ready in case he tears the first), sister has "woaded" the patient from navel to knees, a sterile towel is on the abdomen, another occludes the rectum, the vagina has been swabbed with flavine, and another expert has anaesthetized the patient. It is probable that in these circumstances running in and out of the uterus as advised may not end in disaster.

But what of the occasional obstetrician in the back of beyond who knows that Mr. Stabler cannot reach him and the blanched woman under two hours? Hastily scrubbing up, he pours pure "dettol" on his hands and "washes" till tacky, anxiously eyeing the while inexpert chloroform dripping at one end and red blood at the other. Introducing a hand he separates the placenta all round and delivers it—*horribile dictu*—by pulling on the cord, and *then* feels round for debris. Obviously the uterus cannot invert with the hand in the fundus; the membranes are not more likely to be torn than by fingers scratching about inside; and only *one* introduction is required. One would of course not dare to say this had one not heard it advocated by a most distinguished London gynaecologist.—I am, etc.,

London, E.4. FREDERIC SANDERS.

"Unjustified" Use of d-Tubocurarine Chloride

SIR,—I hesitate, as an obstetrician, to enter into this correspondence between two such experts, but as I understand it the uses of curare in this respect are that (*a*) it greatly diminishes the tendency to spasm, making intubation, if necessary, easier; (*b*) it enables the entire anaesthetic to be conducted on an exceptionally light plane so that the infant, not being "anaesthetized," cries almost as soon as the head is born and the patient almost before leaving the theatre is becoming conscious; (*c*) it "potentiates" the action of the barbiturate, thereby lessening the required dose. These reasons Dr. T. Cecil Gray has already ably expounded. Dr. A. H. Galley (Nov. 22, p. 840) has scarcely viewed the matter from the standpoint of the obstetrician when he states that "the only possible reason for administering curare preparations to caesarean sections must be for its effect in relaxing the tone of the abdominal musculature." In point of fact, while a fair degree of relaxation is obviously desirable in the initial stages of the operation, it is clearly not asked for with the same urgency as in general surgical procedures in the upper abdomen.

In so far as uterine tone is said to be enhanced by this type of anaesthesia, the problems in pure physics inherent in the contracting uterus simplex at the onset of labour are sufficiently complex as surely to make it unlikely that one may justifiably cite a simple relationship between "kemithal"–cyclopropane anaesthesia and the "eyeful of liquor" which incommoded the present P.R.C.O.G. The incident was disturbing but did not necessarily prove very much, and with optimum conditions such an incident could, I imagine, be repeated quite easily under local anaesthesia. The essential point which I would make is that as an obstetrician one bears a heavy responsibility, not for one life but for two. The mother is frequently ill prepared for a major surgical procedure in comparison with what her state of preparedness would have been for most procedures in general surgery, and the influence particularly of the older types of inhalation anaesthesia on the foetus is too well known to need emphasis. The technique that my colleague Dr. Gray described so well in the *Journal* of April 5 (p. 444), and with which I have now had a fair experience in collaboration with him and other expert anaesthetists, seems to me to offer the obstetrician a few more significant advantages than a little added relaxation of the abdominal musculature, which in any case can often be done without in the initial phase of the operation.—I am, etc.,

Liverpool. H. VINCENT CORBETT.

Diabetes Insipidus and Hyperostosis Frontalis

SIR,—I have read with great interest Prof. G. Marañón's article about diabetes insipidus and uterine atony (Nov. 15, p. 769), but I am surprised that he does not discuss the possible significance of the slight frontal hyperostosis disclosed by the radiograph. Could that hyperostosis not be the "non-malignant non-progressive lesion of small size" for which he looks? It is known that patients with hyperostosis frontalis interna have frequently cerebral symptoms and signs and particularly those pointing to the hypothalamic-pituitary region.—I am, etc.,

Harrow Weald, Middlesex. A. LETCHNER.

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Oxytocic Action of Ascorbic Acid

SIR,—Prof. Chassar Moir emphasized[1,2] the proper use of pituitary extract and ergometrine during and after labour. Dale's[3] discovery and Hofbauer's[4] practical application of the remarkable physiological action of posterior-pituitary extract on the gravid uterus, and Dudley and Moir's[5] isolation of ergometrine, are corner-stones in the advance of conservative midwifery.

The dangers of employing pituitary extract for induction and acceleration of labour have been stressed repeatedly. Chassar Moir's golden rules for the use of standardized pituitary preparations should be strictly observed by all who practise midwifery. With considerable interest I have therefore collected experience about the use of ascorbic acid as an oxytocic agent in labour, having had in mind the disadvantages of pituitary-extract preparations in the first and second stage of labour. My observations, which are based on several hundred deliveries, confirm the views of Kappeli,[6] of the gynaecological university clinic in Berne, that ascorbic acid has a distinct influence on uterine contractility.

I found that the time of employment is chiefly the dilatation period. Contractions must be established. It has, therefore, no effect on an inactive uterus. For induction of labour I found it unsuccessful. Ascorbic acid is used in the first stage, cervix 2–3 fingers wide, when uterine contractions are less than one in three minutes and weak. It is administered preferably by mouth, 100 mg. of ascorbic acid for three doses at half-hourly intervals. If there is no effect the drug can be given in three 6-hourly courses within 24 hours. A 1-min. (0.06-ml.) dose of

"pitocin" can be given after the third dose of ascorbic acid if desirable, often with a very notable oxytocic effect. Higher doses of ascorbic acid are useless. Intravenous use may lead to tonic contractions. Intramuscular administration is of no advantage.

Ascorbic acid proved especially useful in patients with uterine inertia, in which posterior-pituitary extracts were contraindicated. There were no ill effects in mother or baby. In malpresentation, trial labour, antepartum haemorrhage, and foetal distress, where the use of other oxytocics needs greatest supervision and caution in dosage, ascorbic acid is safe and deserves a trial before any other oxytocic agent. Toxaemias of pregnancy are a great field for the use of ascorbic acid as an oxytocic.

It is worth noting that, with the above qualifications, ascorbic acid seems to me an active oxytocic drug which is preferable to posterior-pituitary extract, especially for patients with hypotonia in the dilatation period. The object of this communication is to call for further experimental and practical investigations of a relatively simple and safe chemical substance which appears to regulate and stimulate contractions on the already active gravid uterus.—I am, etc.,

London, W.1. W. SPITZER.

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4 *Zbl. Gynäk.*, 1911, **35**, 137.
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Dwarfism, Hormones, and Dieting

SIR,—Dwarfism associated with hypogonadism may be of endocrine origin and may respond to gonadotrophic hormone, testosterone, or anterior-pituitary growth hormone. Preparations of the latter at present available are, on the whole, disappointing, although in October I showed a patient of 15 years of age with infantilism at the Royal Society of Medicine (Endocrine Section) who had grown 3 in. (7.6 cm.) in a few weeks on large doses of growth hormone at a total cost of £60, or $240, the available preparations being of American origin. The local reactions to these large doses—e.g., 5 ml. b.d.—were severe and painful.

In October, 1946, at one of my hospital out-patient clinics I saw a boy of 15, height 4 ft. 6½ in. (138.4 cm.) with hypogonadism, whom I proceeded to treat with thyroid and pituitary growth hormone (by injection) until April, 1947, at the end of which period of six months he had grown 5/8 in. (1.6 cm.). I then lost sight of him for five months, and when he reappeared in September of this year he had grown a further 2½ in. (6.3 cm.) in a period of five months. I assumed at first that he had carried on with the treatment, but I was informed by his mother that he had had no treatment whatsoever but had gone to some relatives on a farm in Ireland and had enjoyed open air and some very good food. In the few months he has been home he has ceased to grow. It is difficult to believe that the growth was unrelated to the period of five months in Ireland.

I am reminded of the work of my old professor, the late Sir Frederick Gowland Hopkins, on the importance of animal proteins and some of the amino-acids essential for growth—e.g., tryptophan and lysine. I am also reminded of the experiments of Corry Mann many years ago (1926), who showed that if the population of a large poor-school were divided into two sections and one half received an extra pint (568 ml.) of milk daily the children in that section grew 1 in. (2.54 cm.) per annum more than those of the control section.—I am, etc.,

London, W.1. S. L. SIMPSON.

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Remuneration of Specialists

SIR,—A factor which should be considered in regard to the remuneration of a specialist is length of the necessary apprenticeship, though responsibility and annual turnover of patients may also be relevant. It is not reasonable for the man who has worked for a year or two at a special subject and obtained a diploma to expect the same returns as the man who has worked for a higher qualification and is prepared to spend possibly ten years earning little and acquiring the experience to establish himself.—I am, etc.,

Lymington, Hants. GEOFFREY HALLETT.

Space for X-ray Departments

SIR,—The carefully thought-out plan for a hospital unit which accompanies the article by Mr. H. J. McCurrich on "A Suggested Hospital Unit" (Nov. 22, p. 832) has reminded me once more of the oblivion into which the Recommendations of the British *X*-Ray and Radium Protection Committee have fallen. This otherwise admirable scheme allows approximately 14 ft. by 11 ft. (4.3 m. by 3.4 m.) for the *x*-ray room and 5 ft. by 5 ft. (1.5 m. by 1.5 m.) for the dark room and a similar size of store room. The Recommendations referred to above stipulate a minimum floor area of 250 square ft. (23.4 sq. m.) for *x*-ray rooms and 100 square ft. (9.2 sq. m.) for dark rooms. It is astonishing that only 154 and 25 square ft. (14.2 and 6.7 sq. m.) respectively should have been allowed.

The author expressly states that the plan does not claim to be perfect in detail and mentions the desirability of having the plaster room and *x*-ray room adjoining. But what interests me is that a plan should be prepared which so flagrantly violates recommendations that are supposed to be accepted by the responsible medical bodies of this country.

Recently another firm of hospital architects raised no objection to a proposal to put an *x*-ray department in a basement until I drew their attention to the existence of the Recommendations. It was then found that the proposal originated with the architects of the Ministry of Health. On pointing out that one of the Recommendations was that *x*-ray departments including dark rooms should not be situated below ground level, the proposal was dropped, but my attention was drawn to the fact that many other hospitals have *x*-ray departments in basements.

Among numerous others the Westminster Hospital, one of the most recently planned and built of large teaching hospitals, has its *x*-ray department below ground level, I am informed. If this is so, it merely emphasizes the extent to which the Recommendations have been forgotten. They are expressly stated to be minimum requirements and not optimum objectives, and I feel that they should be resurrected and enforced in the way that building by-laws are.—I am, etc.,

Richmond, Surrey. DOUGLAS GORDON.

Blepharospasm

SIR,—Among the various tics which we are called upon to treat probably none is more frequent or intractable than the twitching eyelid. Some time ago I was consulted by a patient who was greatly distressed by this condition, which had persisted for nearly a month. He had only decided to get medical advice when on the previous day the ear on the affected side began to ache. When I examined the ear it was full of hard wax, the removal of which was followed by an almost immediate and dramatic cessation of the tic, which has not recurred. Since then I have treated another patient for the same trouble in similar fashion, with almost immediate relief of the condition. In this case, however, there was no accompanying earache, deafness, or tinnitus to guide one.

I am writing this because in such literature as I have by me on the subject the causes of tics are variously listed as errors of refraction, conjunctivitis, carious or unerupted teeth, phimosis, worms, adenoids, and constipation. I find no mention of cerumen auris as an exciting cause, a condition which one may easily fail to consider.—I am, etc.,

West Malvern, Worcs. W. G. SHAKESPEARE.

Health Centres

SIR,—I read with great interest Dr. S. F. Logan Dahne's letter (Nov. 8, p. 744) on the subject of health centres. It seems to me that such a development does give promise of an improvement in the medical services of this country, and it fits in admirably with an idea I have had in mind for some time as to the organization of the hospital service.

For this purpose I should like to see the country divided into areas, each with its base hospital staffed by whole-time consultants and specialists. These would preferably not be on a whole-time salaried basis. The base hospital would be surrounded by satellite (local) hospitals, staffed by such of the local G.P.s as had the desire, ability, and experience to take

up a part-time specialty. A close liaison is a simple matter between the G.P. and the part-time specialist, who both live in the same neighbourhood, and there should also be regular visits by the "part-timer" to the base hospital. These visits would enable him to keep in touch with the appropriate consultant and also to follow up cases which he and/or the G.P. had passed on there. I venture to think that the doctor who sends a case into hospital would then learn much more from doing so than he does at present, when all he gets is apt to be a curt note to say that his patient had a swollen head, has been decapitated, and please send him to out-patients in four weeks.

Part-time specialism does not seem to be in favour in high circles, but I believe it is the best, if not the only, way of maintaining and improving the knowledge, skill, and clinical sense of a large part of the profession, and it should be remembered that however skilled the specialist service may be the patient will not derive full benefit from it unless the G.P. is sufficiently knowledgeable to ensure that he reaches the right specialist at the right moment.

Such a scheme would be far more difficult to initiate than the mere "administrative snuffer" which the present Act inflicts upon us all, but taken in conjunction with Dr. Dahne's proposals it appears to me to offer a much greater prospect of improving the knowledge and skill of the individual doctor, without which surely no improvement in the Health Service of the nation is possible.—I am, etc.,

London, N.W.8. J. H. RANDALL.

Contact Lenses

SIR,—Mr. A. G. Cross (Nov. 22, p. 843) has stated in effect that only 64% of patients wearing contact lenses do so without discomfort. We think that this must refer to prefenestration days. Since the adoption of this technique the percentage has risen considerably, and one of us, who could wear closed contact lenses for only an hour or so, can wear a perforated pair for ten hours or longer. This, we believe, is the usual experience. The rationale of fenestration was explained by Dr. J. Dallos in the *British Journal of Ophthalmology*, 1946, **30**, 607.—We are, etc.,

F. A. WILLIAMSON-NOBLE.
London, W.1. A. RUGG-GUNN.

POINTS FROM LETTERS

Unclean Hairdressers

AURELIA writes: Can nothing be done about the low standard of cleanliness in our post-war hairdressing establishments? I do not know what is done in the barbers' shops, but every time I have my hair done I am shocked at the lack of the most elementary sanitary precautions. The fact that I take my own comb is regarded with disfavour by the assistant, but if I do not do so a seemingly uncleansed comb emerges from her pocket, the pre-war jars of disinfectant being no longer used. When the hair is dried, a dirty-looking net is taken from a grimy box full of nets, clips, pins, etc., and a much-used wad of cotton-wool is placed over one's ears. I shudder to think of the diseases that can, and probably are, conveyed in this way. It is almost as alarming as the elementary way in which cups and saucers and so forth are washed up in restaurants and trains. . . .

Geriatric Department

Mr. L. Z. COSIN (Orsett Lodge Hospital, Essex) writes: The synopsis of my article on "Modern Methods in the Care of the Aged" (*Journal*, Nov. 29, p. 870) failed to mention the other specialists required in a geriatric department. I append a complete list: (1) Physician experienced in the treatment and diagnosis of aged patients; (2) psychiatrist; (3) physician experienced in physical medicine; (4) orthopaedic surgeon; (5) genito-urinary surgeon; (6) general surgical service.

Snoring

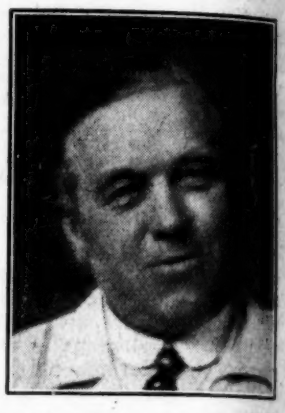
Dr. OSMOND H. BROWN (Guildford, Surrey) writes: As to the horse and cow I am not qualified to speak, but as a close associate of cats for over fifty years I can state as a fact that cats can and frequently do both breathe through the mouth and snore. Other animals in which I have personally observed snoring are dogs, dormice, hedgehogs, parrots, owls, and canaries.

Obituary

SIR JOHN FRASER, Bt.
K.C.V.O., *M.C.*, M.D., Ch.M., F.R.C.S.Ed.

Sir John Fraser, Principal and Vice-Chancellor of Edinburgh University, was one of Edinburgh's most distinguished graduates and inspiring leaders. He died suddenly on Dec. 1 when leaving a meeting which he had been attending at the Old College, having recently resumed his work after a serious and protracted illness.

John Fraser was born at Tain, Ross-shire, in 1885. He graduated M.B., Ch.B. with honours at Edinburgh in 1907, took the degree of Ch.M. with honours in 1910, and was awarded a gold medal for his M.D. thesis in 1912. He studied in Paris and Freiburg, and under Harold Stiles engaged in research on tuberculosis, particularly tuberculosis of bovine origin. His book, *Tuberculosis of the Bones and Joints in Children*, was published in 1914. During the 1914–18 war he served as a captain in the R.A.M.C., was wounded, and was awarded the M.C. and mentioned in dispatches. On his return to Edinburgh in 1918 he became an extra-mural teacher in surgery, and was appointed surgeon to the Royal Hospital for Sick Children and assistant surgeon to the Edinburgh Royal Infirmary. His *Surgery of Childhood* appeared in 1926. His outstanding qualities as a teacher and surgeon were acknowledged when in 1925 he was appointed to succeed Sir Harold Stiles in the regius chair of clinical surgery at Edinburgh University, a post which he held with distinction until 1944, when he was appointed Principal and Vice-Chancellor of the University. In this capacity, in spite of serious ill health, he took a leading part in plans for integrating the development and extension of the University, and a keen interest in all aspects of university life.



Among his many public appointments he was honorary surgeon in Scotland to His Majesty the King, civilian consultant in surgery to the Royal Navy in Scotland, and consultant adviser to the Secretary of State for Scotland on the organization of hospitals in wartime. In 1937 he was honoured with a knighthood, and he was made a baronet in 1943. At the annual meeting of the British Medical Association in Edinburgh in 1927 he was president of the Section of Diseases of Children, and he was vice-president of the same Section at the centenary meeting in London in 1932.

John Fraser was a born teacher, a lucid speaker, a prolific writer, and a master of the art of demonstration. His clinics were popular not only with students but also with graduates from many schools. His surgical skill was widely appreciated, and in addition to his hospital work he had a large private surgical practice, which included many doctors and their families. His operative speed and accuracy of technique were exceptional. He was always unruffled and unhurried and inspired great confidence in his patients and devotion in his staff. Besides being a Fellow of the Royal College of Surgeons of Edinburgh since 1910, he was an honorary Fellow of the American College of Surgeons and also of the Royal Australasian College of Surgeons. As a man, he was unsparing of himself in his work for others, and all those who were privileged to meet him will remember his unfailing courtesy and kindness and his quiet charm of manner. He is survived by Lady Fraser and a son and daughter.

J. B. writes: By the sudden death of Sir John Fraser his alma mater has lost a wise guide and a sage counsellor at a time when wisdom and vision are more than ever necessary in university affairs, and the rich promise of a memorable principalship must remain unfulfilled. There have been many

warm and eloquent testimonies to the brilliance of his many achievements and to his unique technical and intellectual gifts. Where there is no greatness of character, however, there can be no great man; and Sir John possessed in rich measure the qualities of true eminence—a deep spiritual strength, the more real because so devoid of display, and a broad and sensitive humanity. To the young men he gathered round him in the heyday of his distinguished surgical career he was a supreme teacher and an inspiring example. From his lips fell no harsh criticisms or judgments of his contemporaries, for indeed he spoke ill of none. He was devoid of malice, of jealousy, and of envy; all the remarkable energy, the unsurpassed skill, and the exquisite gentleness he possessed he gave freely and fully to his craft. From his mere presence all his patients derived strength and confidence.

As a clinical instructor, even in a university which has never failed to attract eminent teachers of the highest intellectual rank, he occupied a unique position. His classes and his operating sessions were alike crowded, and he was never too busy or too tired to explain and to demonstrate. For young men he set the best of all examples—that of a great surgical craftsman, superb in his gentleness and dexterity, wide in his knowledge and wise in his judgment. In his theatre there were no harsh words, no frivolous remarks; and his influence on surgical practice in many parts of the world, through the medium of the many thousands who flocked to his clinics, is incalculable. If, as Disraeli said, a great man is one who affects the mind of his generation, then Sir John Fraser was indeed pre-eminent. Something of his inspiration and his outlook, his humanity and his kindliness, has been woven into the fabric of many lives. In such a manner the goodness that men do can live after them. If in a cosmopolitan university the great surgical teachers, like Sir John, are clothed in the dignity and heritage of their high calling and serve well its moral and its physical disciplines, they light a beacon which throws its light across the world. Yet his Celtic temperament and his natural humbleness combined to make him a shy, gentle, and retiring man; but to those who chose to breach the barrier of his reserve he offered a rich reward of loyalty and friendship. We who were privileged to work for him would often have liked to show our love for him more than we dared to do; but I think he comprehended more than we thought and his letters often revealed a depth of affection which he could seldom bring himself to show in any other way.

In his home life he was singularly blessed. His wife and he were deeply devoted to each other, and Lady Fraser, to whom our sympathy goes out at this time, played a notable part in a notable career. Those who saw something of them during his recent illnesses were privileged to witness an affectionate understanding which they will not soon forget. This is a personal tribute. Many, like the writer, will to-day mourn the grievous loss of a dear friend, a great surgeon, a good man. The life of Scotland has been nobly enriched by his presence amongst us and saddened by his death.

J. M. G. writes: Sir John Fraser's career was a record of achievement in everything he undertook. He will be remembered as a great surgeon and teacher and for his qualities of character, which endeared him to everyone with whom he came in contact. For nineteen years he upheld and enhanced the reputation of the regius chair of clinical surgery in Edinburgh. When he succeeded Sir Harold Stiles he was truly in the line of the great tradition, for he was the last house-surgeon of Annandale, who had been the colleague and successor of Lister and assistant to Syme. Even as a young house-surgeon Fraser made an impression on his seniors and on all with whom he worked. The late Mr. Dowden foretold a brilliant future for him from the time of their early association in Mr. Annandale's wards. His reputation was finally established when he read his first paper in Edinburgh, at a meeting of the Medico-Chirurgical Society, on tuberculosis of the bones and joints. The suggestion of the president, Sir Montagu Cotterill, that Fraser should be asked to read a further paper on the subject at the next meeting was received with acclamation by all who were present.

With his high sense of duty, which was one of his outstanding qualities, Sir John never spared himself. Few men in our time can have worked harder than he did, or applied themselves more consistently to whatever task came to hand. With his special knowledge of the diseases of children as a foundation, he became, in the best sense of the term, one of the great general surgeons, highly competent in almost every branch of surgery. His operative technique was simple and straightforward, and was combined with a manual dexterity and a sureness and gentleness of touch which could scarcely be excelled. However busy he was, he always seemed to find time to read widely, not only in his own subject but in general literature. The knowledge and culture which he so readily acquired were always at his command, and were invariably apparent in his teaching and in his writings. Throughout his career Fraser's teaching was outstanding in its appeal to the students and for many years also to an increasing number of graduates.

Sir John received many distinctions and honours, but to the last he remained the same, the most unassuming and approachable of men, deprecating his own accomplishments and generous in acknowledging the efforts of others. In his personal contacts he had a charm peculiarly his own, and it is not surprising that he gained without exception the affection as well as the respect of his colleagues. Throughout his active career the calls on his time and energy seemed to be without limit or end. His advice was constantly sought by colleagues and practitioners on behalf of their patients, for they knew that everything that could be done would be done by him, and the patients themselves intuitively felt the utmost confidence when they were under his care. He served on and presided over innumerable committees, and delivered addresses to medical societies on many occasions in this country and abroad.

The honour of being appointed Principal and Vice-Chancellor of the University of Edinburgh in 1944 was accepted by him with a full sense of the responsibility involved. The burden of this office came at a time when he was tired with the strain of the war years, but without hesitation he entered on his new duties with the same energy and devotion which he had shown throughout his surgical career. A few months after his appointment he suffered an illness during which for a few days he was critically ill. It is at such a time that a man's true nature is revealed. Under the most trying circumstances he never complained, but showed a constant courage and gratitude for the efforts made to help him. It was characteristic of him that in these critical days his thoughts were always for others and never for himself. Shortly before his sudden death Sir John attended a meeting of the Council of the Royal College of Surgeons of Edinburgh. His colleagues rejoiced to see him apparently stronger and fitter than he had been. He took an active part in the business of the meeting, but a few minutes after they had parted he passed away in the precincts of the university to which he had dedicated the completion of his life's work.

W. ROWLEY BRISTOW, F.R.C.S.

Major-General D. C. Monro writes: News of the death of Walter Rowley Bristow has just reached us here in the Middle East. He will be sadly missed in various circles, social, sporting, and professional, in all of which he had numerous friends and admirers and many grateful patients. Although I had met Walter Bristow before his Army appointment and have good reason to remember his hospitality, kindness, and encouragement on those occasions, it was not until he became a member of the War Office Consultants panel, and of the surgical sub-committee of which I was chairman, that I got to know him intimately and had an opportunity to appreciate his sterling qualities. Besides being one of the senior orthopaedic surgeons in Britain, he had an international reputation. I remember well an occasion in 1939 when a deputation consisting of senior orthopaedic surgeons, which included Bristow, McMurray, and Platt, practically demanded to see our D.G., then Lieut.-Gen. Sir William MacArthur. The deputation insisted that the role of orthopaedic surgery in the war surgical organization should receive fuller recognition, and warned us that it would be folly to forget the mistakes and lessons—all of which had received somewhat belated recognition—of the 1914–18 war. They pleaded that the teaching of the late Sir Robert Jones, whose breadth of view and forceful character had been such an influence for good at that time, should not go unheeded. This warning was timely, and that this advice was valuable is evident when the results in the two wars are com-

pared. The attainment of such results was mainly due to the work of the surgeons who treated the fractures, but Bristow, by his amazing energy, his zeal, his personality, and his amicable relations and close association with the leaders in orthopaedics not only in Britain but with the Dominion and the Allied Forces, and by his fatherly interest in the work of all his juniors, played a very considerable part in it all.

Not unnaturally, Bristow and I often toured and inspected together. I learnt much from him during our joint ward inspections. The tedium and strain of many a tour by land or air was relieved by his high spirits, his optimism, and his genial companionship. Between visits to centres, when we could relax for a while, I was never short of an opponent or partner for almost any sort of game. Bristow was a keen fisherman, a good shot, and an all-round sportsman. If the game we played had an element of chance in it, so much the better; and how often his good-natured and witty propaganda chat would turn the scales in his favour. Too often, whether he lost or won, he would insist on paying the forfeit himself, and what a wonderful host he was. If he could not be at home with his wife and family of whom he was so justly proud, or fishing or shooting, Bristow was happiest either at work or pitting his prowess and cunning against an opponent in some form of game.

This was the surgical colleague or teacher we all came to respect and admire. Those who could proudly regard him as a friend, and they were many, loved to call him "Rowley." Among his friends and admirers can be numbered many from the lower walks of life, especially in his own London—grand types of the old retainer class, club porters, head waiters, and even taxi-drivers and "Bobbies." These loved "Mr. Bristow" too, either because of some unobtrusive kindness or help, or because they admired his philosophy of life, his zest for living it, or were naturally attracted by his cheery personality. Because our friend "Rowley" has gone and we miss him, I and my friends of the surgical service in the Army want to pay a humble tribute to his memory. To his family, who are most entitled to our sympathy, we commend his philosophy of life.

Prof. K. H. BOUMAN, of Amsterdam, died at his home on Nov. 8. He had been until recently professor of psychiatry and neurology at Amsterdam University for many years.

Dr. Henry Robinson writes: All those who went with the British Medical Association tour to the Annual Meeting at Melbourne in 1935 will hear with deep regret of the death of Prof. K. H. Bouman. In the previous winter the professor and his wife went for a brief holiday tour to the Canary Islands; through meeting there a member of the Association they formed an ambition to make the world tour with the B.M.A. in the following summer. It was learned that this was feasible if he were elected an honorary member of the Association, about which, in view of his very distinguished academic record, there was no difficulty at all. Accordingly Dr. and Mrs. Bouman joined the party, and in a short space of time became two of its most popular members. Both of them spoke English admirably—practically without any foreign accent in Mevr. Bouman's case. On the return journey they broke the voyage home by remaining for a time in the Dutch East Indies; to visit mental institutions there had been the justification for the leave of absence granted to him by Amsterdam University.

Prof. Bouman was 73 at the time of his death: the name means "farmer," and is etymologically similar to the term "Boer" as used in South Africa. In normal circumstances he would have retired on pension some years ago, but the exigencies of war prevented this, and he carried on steadfastly, though many times threatened with death by the Nazis for refusing to carry out their orders. When, at the end of hostilities, relief should have been in sight it was further postponed because the deputy who had been trained up to succeed him was sent to prison for life on a charge of collaboration. Two years ago, after the liberation, Bouman visited London and delivered an address to the Medico-Psychological Society on the hardships and diseases produced among the population of Holland by the Germans, whose aggression and disregard of human rights he had foreseen long before the war broke out. This account of his privations and those of his compatriots produced a lasting effect upon his hearers, all the more so by reason of the grave composure, dignity, and emphasis, without any ostensible expression of rancour, with which it was delivered. To his widow, Mevrouw Wilhelmina Bouman-Slingenberg, the deep sympathy of her many English friends will surely be extended. There were no children of their marriage.

Medical Notes in Parliament

Criminal Justice Bill

Mr. CHUTER EDE on Nov. 27 moved the Second Reading of the Criminal Justice Bill, which was the subject of a leading article in our issue of Nov. 22 (p. 826). Mr. Ede said that the Bill abolished penal servitude and hard labour and also the division of prisoners into first, second, and third divisions. The abolition of penal servitude involved the abolition of the ticket-of-leave system. The Bill proposed to abolish whipping as a punishment to be ordered by the courts. Crimes of violence had increased markedly since 1938 and the Government could not regard the time as opportune for the inclusion in the Bill of a provision for the suspension or abolition of the death penalty. The Government would put their case before the House, but no attempt would be made to coerce the conscience of any member.

Mr. ALLEN noted that there was nothing in the Bill to provide for payment for inquiry by an expert into the mental condition of a child or adult. Viscountess DAVIDSON also remarked that the Bill did not make mention of educational psychologists.

Mr. GAGE asked that allegedly insane people should be given legal aid in the lower court. Dr. MORGAN did not agree. He said that if prisoners were insane or mentally defective what was required was a report by a psychiatrist. Mr. GALLACHER condemned the silent cell and said he had heard prisoners battering against the door night after night. There was no more exquisite torture.

When the debate was resumed on Nov. 28 Mrs. CORBET said that in one prison sick persons were obliged, however ill they were, to get up at 5 a.m. to consult the doctor. Mr. JENNER said the M'Naghten rules were laid down some hundred years ago, and the judges found themselves to-day bound to observe rules which in the opinion of most people concerned were antiquated. The hanging of persons subject to attacks of epilepsy could be altered by having a proper record of an accused man's past. To-day in the prisons the man might be put under observation by a medical officer who had no knowledge of investigating mental deficiency.

Replying for the Government Mr. YOUNGER said that where it was practicable an inquiry into the physical and mental condition of an offender would take place in any institution and not necessarily in a remand centre. Medical personnel would be provided under the National Health Service, but how far it would be possible to provide enough skilled medical officers, psychiatrists, and psychologists no one in the House could say. Mr. EDE promised to see whether an extra half-day could be given for debating the Bill during the Report Stage, and the measure was read a second time without a division.

Purchase Tax on Drugs

When the Autumn Finance Bill was taken in Committee on Dec. 2 Mr. SELWYN LLOYD moved to exclude from the increase in purchase tax drugs and medicines, manufactured or prepared. This point was discussed in an annotation in our issue of Nov. 22 (p. 829).

Mr. Lloyd said that at the moment drugs and medicines were subject to a tax of one-sixth of the wholesale value of the goods, which was now to become one-third. The matter had been dealt with on the last Finance Act. When Mr. Stanley spoke on that occasion he got a promise from the Financial Secretary to the Treasury that during the twelve months after June 17, 1947, the date of that debate, he would look into the matter of drugs and medicines and examine the illogicalities which he admitted to exist. The present was a convenient moment to make a progress report on how far the Financial Secretary had gone. Mr. Selwyn Lloyd went on to say that he had attempted to find out which drugs and medicines were subject to purchase tax. Iodine—a simple medicine very commonly used—was subject to tax. He was surprised that a Government so prone to make cuts should be keen on doubling the tax on a simple antiseptic.

Sir HENRY MORRIS-JONES said some drugs subject to the double tax were a great help in combating sleeplessness. Mr. ERROLL said many of the old and infirm needed medicines and drugs from time to time and the extra purchase tax represented a serious addition to their weekly budget. He reminded the House that the Purchase Tax (Exemption) Order, 1945, exempted penicillin, the sulphonamides, vaccines, and morphine. Parliament taxed the curing of toxic goitre but left free the curing of pneumonia. Matters should be arranged so that all important diseases could be cured without the higher

rate of purchase tax being imposed on the necessary drugs and medicines. The dispensing practitioner who made up medicines for the use of his patients received a certain fixed rate for such medicines; he must bear entirely the cost of the ingredients for these medicines.

Mr. LINSTEAD asked the Chancellor to have a look at the whole operation of the purchase tax as it affected medicine. When the subject was first discussed in the House Mr. Dalton indicated that he could not afford the loss of revenue which the omission of the tax would entail. There was machinery for exempting costly and essential drugs from the tax, but that machinery had been used in a very restrained way. If the Chancellor imposed additional taxation on patent medicines there might be a good deal of sympathy with him. If he desired to do that this was the opportunity for the whole question of the taxation of medicine to be examined.

Sir STAFFORD CRIPPS said there was a long list of exempted drugs which had been dealt with in 1945. The extension of that list to get it on a sounder and better basis had for some time been discussed with the Ministry of Health. He admitted that the present basis did not seem to be wholly logical. This was a matter which between now and next April should be re-examined to exclude those drugs of real importance. By the definition of the Finance Act, 1940, medicines that were made up by a chemist did not attract the tax as a manufactured article, though some drugs in the medicine might be taxed. The incidence was not very heavy, and at present the tax affected what used to be known as patent medicines. Much the majority of the receipts from this tax were really in substitution for the old Medicine Stamp Duty.

Sir Stafford could not believe that the taking of patent medicines without the advice of a doctor was a good way of dealing with the health of any population. It was not always known whether these medicines would accomplish the ends which they were advertised to accomplish, or indeed any ends at all. The Committee could take it that when the list came to be properly considered the bulk of the increase in taxation would fall on goods which used to be subject to stamp duty. Before April he would look into the matter to see whether there could not be more logical and better arrangements about exemptions. They would be much assisted in this matter because the new Health Service Act would be coming into operation. The Ministry of Health would be large users in hospitals and in connexion with other matters.

Mr. PITMAN said that if the Chancellor was going to look at this list he could act quite apart from Budget day and change the list at any minute. If he could not do that now let him look at the grants to doctors under the Health Acts, because grants for the doctors were low enough as it was.

Mr. LINSTEAD said medicines which were prescribed by doctors would in fact attract the tax in so far as they were proprietary medicines. If they set aside medicines prescribed under the National Health Insurance Act, 50% of those prescribed to-day were proprietary medicines which would attract the full 33⅓% tax. The old stamp duty did not apply to medicines which were sent to the chemist to be sent out with a medical prescription. Therefore they would have a heavy tax on medicines which previously had not borne any tax at all.

The amendment moved by Mr. Selwyn Lloyd was defeated by 278 to 131.

Medico-Legal

A BROKEN SURGICAL NEEDLE

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

In a case recently heard at the Liverpool Assizes the question was raised how far it may be the duty of a doctor to press his advice on a reluctant patient. The doctor was repairing a perineal laceration, sustained during childbirth on Oct. 24, 1945, in a girl of 18, when the needle broke and part of it remained imbedded in the tissues. He telephoned for advice to a gynaecologist, who expressed the opinion that the fragment should be left until after she had recovered from the effects of the delivery, and then removed if it had not already been extruded. Fifteen days later the patient complained of discomfort and was advised by the doctor to return in two days, on Nov. 12, to see his wife, also a doctor. This appointment was kept by the patient, but the doctor had forgotten to inform his wife, and made another appointment. The patient attended again, but, according to a Press report,[1] "after sitting in the waiting-room for some time she gathered the impression" that the lady doctor was not available, and so went home, thinking that the doctor had "lost interest" in her case. She did not attend again "because of her shyness" until ten months later, and then only because she was urged to do so by her mother-in-law. She was then admitted to hospital and had the fragment removed. The Court held, on these facts, that the doctor had been negligent, and awarded £75 damages. A stay of execution was granted. The doctor stated in evidence that, when the patient failed to keep her appointment to see his wife, he assumed that she must have gone direct to the surgeon, or changed her doctor.

It was urged for the defence that it was no part of the doctor's duty to "chase the patient," but Mr. Justice Streatfield said, "She was rather shy, timid, and, I think, a little nervous. It was not going to be a serious operation to have the needle removed, but she was afraid it was. The doctor should have reassured her. He made one appointment for her to see a woman doctor, but forgot to make the necessary arrangements. The doctor let the matter slide, did not make sure the needle was removed, and so was guilty of a breach of duty to the patient." Evidence was given at the hearing by a lecturer in pathology at the local university, who said that "the breaking of a needle could easily occur," and that if this happened it was the duty of a doctor to seek "the co-operation of a surgeon to have the needle removed."

It was not suggested that the breaking of the needle was any evidence of negligence, and the doctor did in fact seek, and follow, the advice of a surgeon as to the proper steps to be taken to deal with the imbedded fragment. Where he failed, in the view of the Court, was in that he did not go far enough in his efforts to persuade a timid and reluctant patient to undergo a minor operation. While it would not be practicable to ascertain in every case why a patient fails to keep an appointment or to act on the advice given, this case illustrates the danger of assuming that such a patient needs no further attention.

[1] *Widnes Weekly News*, Nov. 7, 1947.

Universities and Colleges

UNIVERSITY OF OXFORD

In a Congregation held on Nov. 22 the following degrees were conferred:

D.M.—D. M. T. Gairdner (in absence).
B.M.—D. M. L. Doran.

UNIVERSITY OF LONDON

Noel Francis Maclagan, M.D., D.Sc., M.R.C.P., F.R.I.C., has been appointed to the University Chair of Chemical Pathology tenable at Westminster Hospital Medical School from Oct. 1.

UNIVERSITY OF DUBLIN

Joseph Warwick Bigger, M.D., F.R.C.P., professor of bacteriology and preventive medicine and dean of the Faculty of Physic, University of Dublin, was elected to the Senate on Nov. 20, to fill the vacancy created by the resignation of Mr. Justice Kingsmill Moore.

SCHOOL OF PHYSIC, TRINITY COLLEGE

The following medical degrees were conferred on Dec. 3:

M.B., B.Ch., B.A.O.—K. Adler, C. L. S. Archer, Irene R. Christie, R. F. B. Coolican, Kathleen P. E. Crawford, S. Davis, J. R. Evans, Katherine S. P. Hill, Margaret W. Lamb, D. E. Mellon, T. J. Mills, P. R. Oliver, Irene S. Orgel, J. R. F. Smith, F. E. Williams, R. J. Yorke.
M.A.O.—J. A. O'N. Mulcahy.

UNIVERSITY OF WALES

The following candidates for the degrees of M.B., B.Ch. at the Welsh National School of Medicine have satisfied the examiners at the examinations indicated:

MEDICINE.—H. B. Davies, T. Griffiths, H. Harrop-Griffiths, T. R. Hunt, Dilys W. John, H. E. Jones, Margaret E. B. Jones, Margaret O. Jones, J. B. R. Lewis, Constance A. M. Llewellyn, Myfanwy M. G. Prethero, G. G. Richmond, Prudence K. Roberts, Mary Smith, T. M. Warren.
PHARMACOLOGY.—Josephine J. Candy, M. L. Cattell, R. B. Davies, B. M. Frost Smith, B. J. Fudge, S. G. Gang, A. R. Harris, Mary E. V. Jones, Margaret Pugh, J. A. E. Richards, D. B. Scourfield, T. B. Stephens, S. Thomas.

ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW

At a meeting of the Faculty held on Dec. 1 with the President, Prof. G. B. Fleming, in the chair, Graham Herbert Anderson, M.B., Ch.B. (Glasgow), Edward Kenyon Blackburn, M.D. (Sheffield),

Samuel Dunn, M.D. (Glasgow), Rankine Good, M.D. (Shotts), Arthur Thomson Hendry, M.B., Ch.B. (Giffnock), James Hood, M.B., Ch.B. (Lancaster), William Macfarlane Lancaster, M.B., Ch.B. (Glasgow), Thomas Davidson Veitch Lawrie, M.B., Ch.B. (Glasgow), George McCracken, L.R.C.P.&S.Ed., L.R.F.P.S. (Shirlett), Alastair Goold Macgregor, M.B., Ch.B. (Bearsden), Robert Montgomery, M.B., Ch.B. (Rutherglen), Archibald Walker Sloan, M.B., Ch.B. (Bearsden), and George Will, M.B., Ch.B. (Glasgow) were admitted Fellows *qua* physician; John Cuthbertson Jeffrey, M.B., Ch.B. (Glasgow), Alexander Macpherson Keith, M.B., Ch.B. (Glasgow), Shreedhar Shreenivas Kirtane, M.B., B.S. (Edinburgh) Andrew Bruce MacLean, M.B., Ch.B. (Glasgow), Norman McSwan, M.B., Ch.B. (Kilmalcolm), William Albert Watt Maney, L.R.C.P.-&S.Ed., L.R.F.P.S. (Glasgow), Purushottam Bhagwant Sulakhe, M.B., B.S. (Glasgow), Andrew Tomney, M.B., Ch.B. (Glasgow), William Arthur Leigh Tucker, L.R.C.P.&S.Ed., L.R.F.P.S. (London), and Stuart Young, M.B., Ch.B. (Glasgow) were admitted Fellows *qua* surgeon.

EPIDEMIOLOGICAL NOTES

Poliomyelitis

The more rapid decline in notifications mentioned last week has been maintained. Notifications of poliomyelitis for the week ended Nov. 29 were 103 (142) and of polio-encephalitis 3 (3). The figures in parentheses are those for the week ended Nov. 22. It has several times been suggested in these notes that the original notifications tend to overstate the actual incidence of cases in epidemic periods because of the difficulty of diagnosis in the early stages and the desire of practitioners to secure early treatment for their patients. Figures for poliomyelitis recently supplied by the General Register Office for the June and September quarters confirm this view.

Notifications	*Original*	*Corrected*
June quarter	268	244
September quarter	6,192	5,077

Discussion of Table

In *England and Wales* infectious diseases were less prevalent during the week. Decreases were recorded in the incidence of scarlet fever 135, measles 122, acute pneumonia 79, acute poliomyelitis 44, whooping-cough 34, and cerebrospinal fever 10; the only increases were in the notifications of dysentery 46 and diphtheria 25.

A small decline in scarlet fever occurred throughout the country. Although the total notifications of whooping-cough declined, an increased incidence was recorded for London and the south-east region 65, the south midland region 45, and Lancashire 41. The largest local variations in the trend of measles were increases in Northamptonshire 63, and Lancashire 49, and there were decreases in Glamorganshire 74 and Shropshire 63. The rise in the incidence of diphtheria was due to a small general increase.

There were 48 cases of dysentery notified in Berkshire, 13 from Reading C.B., and 35 from Wallingford R.D., where cases reappeared after a lapse of one week. An outbreak involving 18 persons was recorded in Staffordshire, Willenhall R.D. The only other large return for dysentery was Lancashire 20.

The incidence of poliomyelitis, which has been falling since the first week in September, decreased by 44 cases. The largest returns were Lancashire 16, London 13, Middlesex 12, and Yorkshire West Riding 10.

In *Scotland* the incidence of infectious diseases declined. There were decreases in the notifications of scarlet fever 42, measles 46, acute primary pneumonia 29, and diphtheria 14. The only exception to the general downward trend was a rise of 7 in the notifications of poliomyelitis contributed by the western area.

In *Eire* the only variations of any size in the returns of infectious diseases were decreases in the notifications of measles 19 and diarrhoea and enteritis 14. Only 8 cases of measles were notified in Wicklow, Bray U.D., where 78 cases were reported in the preceding week. An increase in the notifications of measles was reported from Dublin C.B. 18, Roscommon, Boyle R.D. No. 1, 14, and Waterford, Dungarvan U.D. 43.

Week Ending November 29

The notifications of infectious diseases in *England and Wales* during the week included: scarlet fever 1,765, whooping-cough 1,513, diphtheria 216, measles 2,772, acute pneumonia 567, cerebrospinal fever 44, acute poliomyelitis 103, dysentery 77, paratyphoid 18, typhoid fever 8.

No. 47

INFECTIOUS DISEASES AND VITAL STATISTICS

We print below a summary of Infectious Diseases and Vital Statistics in the British Isles during the week ended Nov. 22.

Figures of Principal Notifiable Diseases for the week and those for the corresponding week last year, for: (a) England and Wales (London included). (b) London (administrative county). (c) Scotland. (d) Eire. (e) Northern Ireland.

Figures of Births and Deaths, and of Deaths recorded under each infectious disease, are for: (a) The 126 great towns in England and Wales (including London). (b) London (administrative county). (c) The 16 principal towns in Scotland. (d) The 13 principal towns in Eire. (e) The 10 principal towns in Northern Ireland.

A dash — denotes no cases; a blank space denotes disease not notifiable or no return available.

Disease	1947 (a)	(b)	(c)	(d)	(e)	1946 (Corresponding Week) (a)	(b)	(c)	(d)	(e)
Cerebrospinal fever	30	2	21	1	—	43	4	26	2	—
Deaths		—	1				1	1		
Diphtheria	220	23	46	23	2	319	12	107	39	12
Deaths	2	1	—	—	—	5	—	1	—	—
Dysentery	141	17	15	—	—	69	21	28	3	—
Deaths				—	—				—	—
Encephalitis lethargica, acute	3	—	—	—	—	2	—	—	—	—
Deaths		—					—			
Erysipelas			24	12	1			43	12	1
Deaths		—					—			
Infective enteritis or diarrhoea under 2 years				39					61	
Deaths	57	8	16	9	3	64	10	14	16	1
Measles*	2,233	120	178	258	5	5,428	215	301	57	47
Deaths	2	—	3	1	—	1	—	1	—	—
Ophthalmia neonatorum	48	3	4	—	—	61	6	23	—	—
Deaths										
Paratyphoid fever	4	—	—	—	—	20	2	—	—	—
Deaths	—	—	—	—	—	1	—	—		—
Pneumonia, influenzal	503	31	5	2	4	708	54	12	1	6
Deaths (from influenza)†	10	1	—	—	—	18	3	—	—	—
Pneumonia, primary			292	14				339	16	
Deaths		47		11	8		45			13
Polio-encephalitis, acute	3	1				—	—			
Deaths		1					—			
Poliomyelitis, acute	142	13	25	6	3	16	—	2	16	—
Deaths		2					—			
Puerperal fever		1	8		—		3	11		—
Deaths										
Puerperal pyrexia‡	100	11	2	—	2	124	10	9	1	—
Deaths		—					—			
Relapsing fever	1	—			—	—	—			—
Deaths										
Scarlet fever	1,812	132	311	52	44	1,402	102	338	37	45
Deaths	—	—	1	—	—	—	—	—	—	—
Smallpox	—	—	—	—	—	—	—	—	—	—
Deaths				—	—				—	—
Typhoid fever	3	—	—	5	—	3	—	—	14	2
Deaths	—	—	—	—	—	—	—	—	—	—
Typhus fever	—	—	—	—	—	—	—	—	—	—
Deaths				—	—				—	—
Whooping-cough*	1,183	86	46	31	2	1,773	106	205	43	31
Deaths	1	1	1	—	—	11	—	—	—	3
Deaths (0–1 year)	359	52	85	33	11	397	70	71	30	
Infant mortality rate (per 1,000 live births)										
Deaths (excluding still-births)	4,822	799	684	197	142	4,779	753	632	183	151
Annual death rate (per 1,000 persons living)			14·2	12·4				13·9		
Live births	7,465	1163	950	309	242	8,867	1389	1134	328	251
Annual rate per 1,000 persons living			19·1	19·5				22·8		
Stillbirths	198	37	34			294	38	48		
Rate per 1,000 total births (including stillborn)			35					41		

* Measles and whooping-cough are not notifiable in Scotland, and the returns are therefore an approximation only.

† Includes primary form for England and Wales, London (administrative county), and Northern Ireland.

‡ Includes puerperal fever for England and Wales and Eire.

Medical News

Dr. Charles Bolton, C.B.E., F.R.S., F.R.C.P.

We announce with regret the death, on Dec. 6, of Dr. Charles Bolton, C.B.E., F.R.S., F.R.C.P., consulting physician to University College Hospital and Fellow of University College, London.

Moray Lodge Sick Bay

A sick bay was opened on Dec. 4 at Moray Lodge, Campden Hill, Kensington, London, W., for civil servants of the lower-paid groups who are appointed to posts in the London area and who live in hostels or lodgings. The sick bay will be administered by the Ministry of Health; the British Red Cross Society will be responsible for its day-to-day management; and the Treasury Medical Adviser and his staff will act as medical officers. While private doctors will be free to visit their patients in the sick bay this will not always be necessary since medical officers will be available on the spot. No case of serious or notifiable infectious disease will be accepted at the sick bay, its function being to deal with the "home nursing" type of case only.

Common Cold Research

More volunteers are required for the experiments which for the past eighteen months have been conducted by the Common Cold Research Unit set up at the Harvard Hospital, Salisbury, by the Medical Research Council and the Ministry of Health. It was emphasized when the investigations started that dramatic results could not be expected, but the work is making steady progress. It has been established that the virus is about the size of the influenza virus, and that it can withstand freezing at temperatures as low as −70° C. Attempts to grow the virus in the laboratory have so far proved unsuccessful. Ten-day sessions for which volunteers are required next year are the periods beginning Jan. 14 and 28, Feb. 11 and 25, March 10, April 14 and 28, May 26, and June 9. People of either sex between the ages of 18 and 40 are wanted, and full details may be obtained from the Medical Officer, Harvard Hospital, Coombe Road, Salisbury.

British Association of Allergists

At a meeting held at Oxford on Nov. 15, it was decided to form a British Association of Allergists. The first general meeting of the association will be held at St. Mary's Hospital, Paddington, London, W., on Saturday, Jan. 24, when the speakers will include Dr. John Freeman and Mr. Frank Coke. Further particulars of the association may be obtained from the secretary (Dr. A. W. Frankland), The Wright-Fleming Institute of Microbiology, St. Mary's Hospital, Paddington, London, W.2.

Yorkshire Society of Anaesthetists

The Yorkshire Society of Anaesthetists has been formed with the object of promoting fellowship and scientific advance in the subject, and an inaugural meeting was held recently at Leeds, under the presidency of Dr. S. T. Rowling. Any doctor who is interested in the society and who did not know of the first meeting should write for particulars to the honorary secretary, Dr. R. C. Lawrence, 6, Wedgewood Grove, Roundhay, Leeds, 8.

Tuberculosis Fellowships

The National Jewish Hospital at Denver announces that Fellowships for postgraduate study in tuberculosis and allied diseases will be granted for three-months, six-months, or one-year periods. Information regarding the Fellowships can be obtained from Dr. Edgar Mayer, chairman of the National Medical Advisory Board, National Jewish Hospital at Denver, 470, Park Avenue, New York, N.Y., or Dr. Allan Hurst, medical director, National Jewish Hospital at Denver, 3,800, East Colfax Avenue, Denver 6, Colorado, U.S.A.

Unification of Pharmacopoeias

The first meeting of the Expert Committee on the Unification of Pharmacopoeias—a committee of the World Health Organization—was held at Geneva on Oct. 13–17. Dr. C. H. Hampshire (Great Britain) was elected chairman. The intention is to produce an international pharmacopoeia whose scope in the first place would be limited to drugs considered essential in medical practice, and 244 drugs were selected from a list of 534 for immediate attention. The preparation of draft monographs and the carrying out of research were allocated among the members present. In view of the amount of work required the Committee recommended that at least three additional members be appointed and that a unified secretariat should be formed.

William Gibson Research Scholarship

The Royal Society of Medicine has awarded the William Gibson Research Scholarship to Dr. Alice Palmer, of Sydney, Australia, for her proposed research on the circulation in pregnancy.

Colony of Aden

Edgar Cochrane, M.D., has been appointed a member of the Executive Council of the Colony of Aden.

Change of Address

Messrs. Burroughs Wellcome and Co. announce that from Dec. 15 the address of their Home Division will be 183–193, Euston Road, London, N.W.1 (Telephone: Euston 4477). The same address will apply to their Overseas Division from Dec. 21.

Wills

Dr. Walter Dickson, Ealing, W., who died on July 6, left £67,039; he left £500 to the Royal Medical Benevolent Fund. Dr. John Alexander Neilan, for some years M.O.H. for Seaham, left £6,208. Dr. Phillip William McCrea, of Bristol, who died intestate, left £178. Dr. Edward Theodore Withington, of Oxford, the well-known medical historian, who died on April 20, left £20,552; he left £100 to the Royal Medical Benevolent Fund.

COMING EVENTS

Royal Microscopical Society

A meeting of the Royal Microscopical Society will be held at B.M.A. House, Tavistock Square, London, W.C., on Wednesday, Dec. 17, at 5.30 p.m., when Mr. Basil Wright, president of the Scientific Film Association, will describe the aims and objects of the association; Mr. A. F. W. Hughes will show films, including "Tissue Culture by Phase-Contrast"; and Dr. Adrianus Pijper's film "Shape and Mobility of Bacteria" will be exhibited.

Bearsted Memorial Hospital

The opening ceremony of the new building of the Bearsted Memorial Hospital in Lordship Road, Stoke Newington, London, N., will be performed by Viscountess Bearsted, president of the hospital, on Wednesday, Dec. 17, at 3 p.m. The hospital is open to patients irrespective of race or creed, and emergency cases and abnormalities may be referred to the board for admission and antenatal treatment by the hospital's consultant obstetric staff.

Pan-American Association of Ophthalmology

The Third Pan-American Congress of Ophthalmology will be held at Havana, Cuba, from Jan. 4 to 10, 1948, when it is anticipated that about 1,000 eye specialists will attend the sessions at the University of Havana School of Medicine. A programme of more than forty formal papers has been arranged, with speakers divided about equally between physicians of the northern half of the hemisphere and those of the Latin-American countries. In addition to the contributions by members there will be several by specially invited guests, including Sir Stewart Duke-Elder (London), who will speak on "Penicillin in Ophthalmology," and Dr. Elizabeth Cass (Gibraltar), who will discuss strabismus.

SOCIETIES AND LECTURES

ROYAL SOCIETY OF MEDICINE

General Meeting of Fellows.—Tuesday, Dec. 16, 5.30 p.m. Ballot for election to the Fellowship.

Section of Pathology.—Tuesday, Dec. 16, 8.15 p.m. Communications by Dr. A. Glücksmann: Quantitative Histological Examinations of Serial Biopsies in Relation to the Radiotherapy of Epithelial Tumours. Dr. G. Payling Wright: The Action of Tetanus Toxin on the Rabbit Iris. Dr. J. Holborow: Effects of Penicillin on the Nasopharyngeal Flora.

Section of Dermatology.—Thursday, Dec. 18, 5 p.m. (Cases at 4 p.m.)

Section of Obstetrics and Gynaecology.—Friday, Dec. 19, 8 p.m. Discussion: Urological Problems in Gynaecological Surgery, with Special Reference to the Vesicovaginal Fistula and the Divided Ureter. Openers: Mr. Everard Williams, Miss Catherine Lewis, and Mr. Ogier Ward.

EDINBURGH CLINICAL CLUB.—At B.M.A. Scottish House, 7, Drumsheugh Gardens, Edinburgh. Thursday, Dec. 18, 8 p.m. Dr. H. M. Traquair: The Lazy Eye. A discussion will follow.

EUGENICS SOCIETY.—At Royal Society's Rooms, Burlington House, Piccadilly, London, W., Tuesday, Dec. 16, 5.30 p.m. Dr. J. A. Fraser Roberts and Dr. Eliot Slater: Genetics, Medicine, and Practical Eugenics. All interested in the subject are invited to attend.

HUNTERIAN SOCIETY.—At Talbot Restaurant, London Wall, E.C., Monday, Dec. 15, 7 for 7.30 p.m. Dinner-meeting. Discussion: Menstrual Disorders in Relation to General Medicine. To be opened by Mr. Aleck Bourne, Dr. Edward Sharp, and Mr. John Howkins.

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE, 28, Portland Place, London, W.—Monday, Tuesday, and Wednesday, Dec. 15, 16, and 17, 3 p.m. Harben Lectures by Prof. E. D. Adrian, O.M., M.D., F.R.S., F.R.C.P.: The Organization of the Nervous System.

POSTGRADUATE DIARY

LONDON CHEST HOSPITAL, Victoria Park, E.—Friday, Dec. 12, 6 p.m. Mr. S. C. Suggit: Common Lesions of the Glottis. (*Change of lecturer and subject.*) Friday, Dec. 19, 5 p.m. Dr. Franklin Wood: *X*-ray Kymography of the Heart and Lungs.

LONDON SCHOOL OF DERMATOLOGY, 5, Lisle Street, Leicester Square, W.C.—Tuesday, Dec. 16, 5 p.m. Dr. J. E. M. Wigley: The Pemphigus Group of Eruptions.

A two-months postgraduate course in surgery will be held at the Royal College of Surgeons in Ireland starting on April 12, 1948. The number of students is limited to 30 and the fee is 20 guineas. Students may enrol now with the Registrar, Royal College of Surgeons, St. Stephen's Green, Dublin.

APPOINTMENTS

LONDON COUNTY COUNCIL.—The following appointments have been made in the Council's mental health services at the hospitals indicated in parentheses: *Physician Deputy Superintendents*, J. C. Batt, M.D., M.R.C.P., D.P.M. (St. Ebba's); D. Shaw, M.D., M.R.C.P., D.P.M. (Sutton Emergency).

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Jarratt.—On Nov. 28, 1947, at King's College Hospital, Denmark Hill, S.E., to Mary, wife of Dr. E. W. Jarratt, a son.

Morles.—On Nov. 22, 1947, at Albion House, Faversham, to Joan (*née* Cannon, M.B., Ch.B.), wife of Dr. Alexander Morles, a daughter.

Petit.—On Nov. 28, 1947, to Joan Lamplugh, M.B., Ch.B., wife of Joseph Petit, of Tanganyika, a daughter—Anne.

Shaw.—On Nov. 21, 1947, at Grove House Nursing Home, Norwich, to Jean (*née* Hart), wife of Richard E. Shaw, F.R.C.S., a son

Todd.—On Nov. 28, 1947, at the Private Hospital, Leicester, to Eileen (*née* Gilbert), wife of R. McLaren Todd, M.D., M.R.C.P., a son—Hugh Ronald McLaren.

Trussell.—On Nov. 29, 1947, at South London Hospital, to Lily (*née* Chant, B.Sc.), wife of Sq.-Ldr. R. R. Trussell, R.A.F.V.R., a daughter.

Zaki.—On Nov. 30, 1947, at Private Clinic Nursing Home, 35, Drumsheugh Gardens, Edinburgh, to Irene (*née* Hope), wife of Dr. Y. E. Zaki, a son—Stuart Swinton.

DEATHS

Bolton.—On Dec. 6, 1947, in London, Charles Bolton, C.B.E., D.Sc., M.D., F.R.C.P., F.R.S.

Downton.—On Dec. 2, 1947, at Hornsey Central Hospital, Arthur Sydney Downton, M.R.C.S., L.R.C.P., aged 68.

Fleming.—On Dec. 5, 1947, at Innerhadden, Kinloch Rannoch, Robert Alexander Fleming, LL.D., M.D., F.R.C.P., F.R.S.Ed., Surgeon, H.M. The King's Bodyguard for Scotland.

Forbes.—On Nov. 27, 1947, at 9, Albyn Terrace, Aberdeen, Charles Forbes, O.B.E., M.B., Ch.B.

Fraser.—On Dec. 1, 1947, Sir John Fraser, Bt., K.C.V.O., M.C., LL.D., M.D., F.R.C.S.Ed., Principal and Vice-Chancellor, University of Edinburgh.

Hegarty.—On Dec. 8, 1947, at 8, Ravenslea Road, London, S.W., Patrick Nicholas Hegarty, L.R.C.P.I.&L.M.

Howard.—On Nov. 26, 1947, outside his home, "Pleasaunce," Beaumont Rise, Marlow, Bucks, Robert Howard, M.B.E., M.D., aged 75.

Jackson.—On Dec. 1, 1947, after an accident, at Manchester Royal Infirmary, William Ferriday Jackson, M.B., Ch.B., aged 74.

Lacey.—On Nov. 29, 1947, at Capetown, Bernard Warner Lacey, M.B., B.S., of 181, Herbert Road, Woolwich, S.E.

Masson.—On Dec. 7, 1947, at Southdene, the Shrubberies, South Woodford, E., Hamish Falconer Masson, F.R.C.S.Ed.

Moffat.—On Nov. 15, 1947, at Bulawayo, S. Rhodesia, Robert Unwin Moffat, C.M.G., M.D., Colonial Medical Service, retired.

Moore.—At "Blairfinde," Greystones, Co. Wicklow, George Peirce Moore, M.D., aged 77.

Scott.—On Nov. 20, 1947, at 13, Southernhay West, Exeter, Robert Scott, M.B., Ch.B.

Smith.—On Dec. 6, 1947, at "Maritzburg," Chipping Norton, Oxon, Thomas St. Clair Smith, M.B., aged 71.

Thomson.—On Dec. 2, 1947, at 83, Duke Street, London, W., William Brown Thomson, M.D., aged 68.

Young.—On Nov. 20, 1947, John Miller Young, M.C., M.B., D.P.H., aged 56.

Any Questions?

Diet in Pre-eclampsia

Q.—*What are the essential features of the diet in cases of albuminuria of pregnancy?*

A.—It is assumed that the term "albuminuria of pregnancy" is used to mean pre-eclampsia. Although it is possible to make some general observations on diet in this disease, each case deserves individual consideration. Starvation should be avoided except perhaps for short periods in severe cases when eclampsia is threatening. Overeating also should be discouraged and the total intake should be average, bearing in mind that the patient is confined to bed—say 2,000 calories a day. Carbohydrate foodstuffs should be given freely, in the form of glucose if necessary. Fats should be taken in moderate amounts only. The traditional low-protein diet is fast losing favour. There is, perhaps, something to be said for limiting the intake of red meat, but other protein foods—milk, eggs, etc.—should be encouraged. Indeed in some cases in which oedema is associated with hypoproteinaemia large amounts of protein are required. Vitamins A, B complex, C, D, and possibly E are important, and if the diet is not rich in these they can be given in the form of supplementary concentrates. A good supply of calcium is also desirable. Table salt should be excluded from the diet so far as possible, and this means excluding foods cooked or preserved in salt. The harmful ion is sodium, and care is necessary to see that the patient does not take this in any other form—for example, mixtures given for indigestion. The intake of fluid is also important, particularly if it is impossible to exclude sodium from the diet completely and if oedema is a prominent feature of the case. In such cases the amount of fluid permissible can be gauged roughly by the output of urine during the previous twenty-four hours, and should not exceed this.

Dietetic restrictions (except in respect of fluid and salt) at present play a relatively unimportant part in the treatment of pre-eclampsia, and the emphasis is on rest in bed. With the present system of rationing in force there is little danger of overeating, and most patients can safely be told to eat their full allowance of all foodstuffs.

Prevention of Venereal Disease

Q.—*Is the application of penicillin ointment to the glans penis and meatus after sexual intercourse a certain preventive of venereal disease?*

A.—The answer is in the negative. Penicillin cream applied immediately after sexual intercourse would probably destroy all or most of any spirochaetes or gonococci on the surface but might not reach organisms which had penetrated into the tissues; naturally it would not protect against those forms of V.D. the organisms of which are not susceptible to penicillin. It seems doubtful whether penicillin applied locally would be any more effective in preventing the development of V.D. than other ordinary hygienic measures, such as thorough washing with soap and water or bathing with mild antiseptics. In all probability gonococci penetrate some distance into the male urethra during sexual intercourse and so would be out of reach of local applications other than irrigating fluids. There is no *certain* preventive of venereal disease except the avoidance of any possible contact with the various causal organisms.

"Privileged Communications"

Q.—(*a*) *In the middle of 1946 two women came to blows. One of them retired to bed, and was examined by her own doctor the next day. In view of the possible legal proceedings the uninjured person called in a second doctor, who, at the request of the first doctor and with the patient's consent, examined the latter and was paid a fee. Twelve months later the solicitor for the defendant (uninjured person) applied to the second doctor for a detailed report of his examination of the plaintiff ("injured" party). Should a report be forwarded to the solicitor?*

(*b*) *After the death of a patient from urogenital tuberculosis an insurance agent asked for a report on the patient's medical*

history, as only two years previously the man had been insured, without medical examination, by a relative, and the company felt this early claim needed investigation. Would a report under these circumstances be regarded as a "privileged communication"?

A.—(*a*) It is quite in order for the second doctor to send a report to the defendant's solicitor. The patient, in giving consent to an examination by the second doctor, and presumably knowing that he was acting on behalf of the defendant (otherwise this consent would be invalid), has given an implied consent to the communication of the results of the examination to the defendant and also to the defendant's solicitor. Such a report is privileged—that is, if given *bona fide* (without "malice") it will not be held to be defamatory of the plaintiff.

(*b*) The doctor should not send any report to the insurance company without the written consent of the deceased patient's executors (if he made a will) or administrators (if he did not). In order that such consent should be valid they should be fully informed of the circumstances so that they understand that the insurance company is seeking grounds to repudiate the policy for non-disclosure. Provided the doctor obtains such consent his report will be a privileged communication.

Raspberry-leaf Tea

Q.—*Many midwives tell their antenatal patients to drink raspberry-leaf tea. Is it any good, and if so in what way?*

A.—Raspberry-leaf tea has long been used as a herbal remedy to allay labour pains and relieve dysmenorrhoea. In 1941 Burn and Withell (*Lancet*, **1**, 1) showed that extracts of raspberry leaves contain a substance—fragarine—that relaxes the uterine muscle of the non-pregnant cat. A relaxing action on the human pregnant uterus was demonstrated by Sir Beckwith Whitehouse (*B.M.J.*, 1941, **2**, 370). Crude raspberry-leaf tea was used at about the same time in a Worcestershire maternity hospital, but no results were ever published. Since then little has been heard of this concoction. The dose usually recommended is 10 to 20 oz. (28–56 ml.) of a 5% infusion of dried leaves in hot water. It is difficult to see how relaxation of the uterus will help a normal labour, unless the active principle in raspberry leaves acts mainly on the os and the lower segment. Conceivably it might have some application in the management of abnormal labour due to a rigid cervix or excessive uterine contraction, and in the treatment of spasmodic dysmenorrhoea.

Absorption of Liquid Paraffin

Q.—*Am I right in thinking that, though ordinary medicinal paraffin is not absorbed, when it is emulsified it is absorbed by the villi and laid down in the fat stores, whence it cannot again be mobilized, and that consequently the giving of paraffin emulsion as a laxative is unwise?*

A.—Liquid paraffin can pass through the intestinal wall of the rat if very finely emulsified, oil globules of a diameter greater than 0.5 μ not being absorbed. The oil is then carried by the lacteals to the fat depots, without passing through the liver, according to the views of Frazer and his colleagues. It is not likely that medicinal paraffin emulsions contain globules small enough to be absorbed, and they may therefore continue to be regarded as simple intestinal lubricants, apart from the fact that we have no reason to believe that deposition of small quantities of paraffin in the fat depots is in any way positively harmful. However, the ingestion of liquid paraffin frequently or in large quantities may have an adverse effect on the body's vitamin-A status, for much of our vitamin A is available to us from the conversion of carotene in vegetable foods, and the absorption of carotene is seriously reduced by the presence of excessive hydrocarbon in the alimentary tract.

Dercum's Disease

Q.—*Can the diagnosis of Dercum's disease be made clinically and is there any specific hormone treatment for it?*

A.—Before making the diagnosis of Dercum's adiposis dolorosa in an indefinite case it is advisable to remove one of the lumps for microscopical examination. The symmetrical deposition of fat, and its painful character, may be met with in varying degrees in all types of adiposity. There is no specific hormone therapy, but the usual treatment for adiposity—diet, diuretics, and moderate doses of thyroid—may be helpful.

Classification of War Wounds

Q.—*What, if any, work has been done on the classification of military casualties during the recent war? I should like to know whether there is any classification of wounds along the lines of the length of time a patient is militarily unfit; also whether any surveys have been made in order to classify wounds statistically in "weapon groups"—that is, wounds caused by shell-fire, mortar-fire, high-velocity bullets, mines, etc. Is there any well-established criterion of wound severity based on the transfer of energy, or rate of transfer of energy, from a missile to the human body?*

A.—A certain amount of work has been done by the statistical branch of the Army Medical Department along the lines indicated in this question—that is, classification of wounds according to the length of time a patient is militarily unfit. These figures, which are based on the results following the first two months after the Normandy invasion, are to be found chiefly in the War Office *Monthly Bulletin of Health Statistics*, 9th and 11th issues (July and September, 1945). Regarding the second part of the question—the classification of wounds into "weapon groups" and the relation of the transfer of energy from a missile to its effect on the human body—this has been dealt with at some length in an interim report of the Military Operational Research Unit (August, 1946), to which is attached a good bibliography on this and related subjects.

Toxicity of Moth-balls

Q.—*Recently I saw an infant who had eaten about one-quarter of a moth-ball, apparently without ill effect. What are the possible toxic effects of moth-balls and what is the treatment?*

A.—Moth-balls are nowadays made of naphthalene, though they used to be of camphor. Naphthalene has a very low toxicity because little is absorbed, but huge doses may produce parenchymatous nephritis. In doses of 3–12 gr. (0.2–0.8 g.) naphthalene is used as an intestinal disinfectant and vermifuge. The *Extra Pharmacopoeia* says that 2 g. over the course of two days has proved fatal to a 6-year-old child, and suggests as treatment that the stomach should be emptied by an emetic or stomach-tube; that a purgative dose of magnesium sulphate and demulcent drinks should then be given, but no oils or fats.

NOTES AND COMMENTS

Reflections of a Haemophiliac.—Mr. WILLIAM CAMP (Long Ditton, Surrey) writes: I am a haemophiliac of 52 years of age. . . . During the period from my birth until I was over 30 years of age I had spent over 20 years in hospital. I had almost no schooling and my education was very little, so please forgive me if my writing becomes confused. Apart from this awful haemophilia I don't know what it's like to feel "off colour.". . . Over 50 years ago my brother bled to death through circumcision. . . . When I was born my mother was a widow and I was brought up in the world's worst slum tenements, in Islington. My mother was ignorant about the complaint. I spent my early childhood in the tiny slum courtyard with hundreds of other kiddies. I can just remember being booted around and being bashed about. My playthings, I recall, were pieces of broken coloured glass and rusty tin cans. Lumme! I must have spent the first 16 years of my life in hospitals. I can just remember when I was about 10 years old I had a tooth drawn. I remember blood, blood, blood, day and night, night and day, until I was picked up somewhere and taken to hospital. At 16 I was ready to face the world alone—ignorant, and badly crippled in my legs through continuous painful swellings in my knees. I can remember seeing my mother once before I took on the whole world alone. I can just remember her clasping my cut thumb and plastering on to the cut a thick dirty old cobweb which she had pulled from the corner of her "sitting-room." (The sitting-room was also the dining-room and bedroom and, I believe, the lavatory for four of us.)

My mother told me that I was a "bleeder." I didn't quite know what that meant, but I believe that I thought that it was my religion. I soon found out! One of my first jobs was in a glass-making factory. At dinner-time we used to stop in the workshop and the men used to throw old sacks and their coats on to piles of splintered glass. I can't remember any of them ever being cut. Neither was I. . . . Once I worked in the kitchen of a large

institution. Speed was the motto. The chef took a liking to me and one day he said that he would make me "the fastest man in the country at chopping up runner beans." The secret was to have a carving knife with an edge like a razor, and to slice the bean close up to the fingers. That time I "bandaged" my cut thumb with a good blob of dough about as big as a hen's egg. I changed the "dressing" every 2 hours for about a week. I kept the blood-sodden dough out of sight as much as I could because I was shy of telling people that I was a "bleeder." . . . I am very poor, yet I should bet that no living soul in this wide world has been shown greater kindness and sympathy than I have received from doctors and nurses. If the nurses have been angels to me (and they have, indeed), my doctors have had a very large dose of the "divine" about them. More than half a dozen doctors have pulled me back from the grave. Why? I've been a bloody nuisance to them most of my life. . . . Why do they do it? It's splendid! It's magnificent! It's superb! It's a miracle! It's—being a doctor. It's the quality of God in man. . . .

I can remember now how, about 30 years ago, I had been bleeding for about 10 days. Doctor said, I believe, "If it doesn't stop soon I shall have to cut one of your veins and let your blood mingle with his"—he said that to the sister, a sweet, lovely girl. She said to him, "Cut where you like. Start now!" That horrified me. I thought that I'd rather do anything than see her be maimed for me. I couldn't think what to do. So I stopped bleeding. . . . I remember how, after bleeding in my tongue for 12 days and nights, I walked and walked all night through with my tongue hanging right out—12 hours a night for 12 nights in the freezing air. The ambulance took me to hospital. I remember the shock when the doctor told me that he had given me snake poison.

I remember how a beautiful, wonderful woman fell in love with me about 20 years ago. I told her everything I knew about my haemophilia. She said, "Right, we get married to-morrow." That was the biggest shock of all. She still loves me. . . .

A long time ago I read an article in some English health journal dealing with "selective breeding" in human beings. . . . They advocated the sterilization (or asphyxiation) of the unfit. Haemophiliacs were about the first on the list to be sterilized. I am *not* sure about this, but I believe that 20 years ago if I knew as much as I now know I would have asked for sterilization.

I have a son 18 years of age. He is 6 feet tall and is classified A1 in the Army. . . . Through hard study and a brilliant intellect he has put himself on the road to becoming one of the finest mathematicians in the country one day. . . . Lucky that I had a boy? Shouldn't he have been born? I have another son of 13 years. He has only had measles. I have a third son aged 7. So to the eugenists I would say, "So what?" Lucky to have 3 boys? I don't feel clever over the fact that my children are boys. I'm not clever. Are the eugenists so very hot? . . . I've got through so far—thanks mainly to my wife and to your wonderful profession.

Pink Disease.—Dr. A. E. BERNSTIEN (Liverpool) writes: It was with interest that I read the reply by Dr. G. M. B. Hales (Nov. 29, p. 896) to a correspondent who asked advice about a case of pink disease. He mentioned that he has treated these cases with intramuscular injections of liver extract and vitamin B twice weekly. I have just had a case of a baby of 10½ months which at three months of age started with diagnosed pink disease and gradually lost weight all the time since then. When the child came to me it had all the signs of pink disease and was in a very sorry state. I treated the case with liver extract and vitamin B in a similar manner to that which Dr. Hales describes, with the exception that I added hydrochloric acid by mouth and calcium by injection. The results were surprisingly good. The child started to gain weight from the first three or four injections, and there was a complete loss of irritability. I found that I could finish with the child after about fourteen injections.

Food Allergy.—The adviser responsible for the answer to a question about food allergy which was recently criticized by Dr. John Freeman (Nov. 29, p. 896) writes: Dr. Freeman's contributions . . . in the past to our knowledge of hay-fever are so outstanding that his present statements on food allergy may be taken by your readers to be a reflection of present-day views on the management of an allergic patient. This, however, is unfortunately not true. The statements, "The way to test is by a skin test with egg protein; this is quite reliable for finding a positive or negative to that particular sensitivity . . ." and "trial dieting is very fallacious . . ." are quite contrary to modern views as expressed in standard books on allergy, for example, *Allergy in Theory and Practice* by R. A. Cooke; *Clinical Allergy* by A. H. Rowe; *Allergy in Practice* by S. M. Feinberg; *Clinical Allergy* by L. Tuft; *Allergy in Practice* by W. T. Vaughan; others could be mentioned, as well as innumerable articles on the same subject. In fact it is the undue reliance on the results of skin tests which has brought discredit on much of the work done on allergy in the past. All these books agree that it is only by careful trial dieting that food sensitivities can be found and proved beyond all doubt. May I quote from the preface of Rowe's book?—"The frequency of the negative skin reaction in food allergy and the fact that positive tests are only important when checked by clinical trial have become assured. . . ." Finally, everyone will not agree with Dr. Freeman's statement, "The child can be desensitized with egg protein." Chobot, in the chapter on food allergy in *Allergy in Theory and Practice*, by R. A. Cooke, writes, "Treatment by desensitization, so-called . . . is uncalled for and ineffective . . ." and "oral therapy with drop-by-drop increases has never been proven to produce the tolerance attributed to it but which nature unaided will provide in practically 90 to 95% of the cases." These are views with which the writer at least is in profound agreement.

Prophylaxis of Dental Caries.—Mr. R. B. D. STOCKER, L.D.S. (London, N.W.), writes: Your answer to a correspondent on this subject (Nov. 29, p. 895), while disposing of the suggestion that vitamin-D therapy might be useful, gives no positive advice at all. It is true that no single preventive measure except local fluoride application or any combination of preventive measures has yet been proved to be effective by rigorously controlled human experiments. Nevertheless there is ample experimental and other evidence to justify treatment which can confidently be expected to lessen caries in young adolescents. Local applications to the teeth of sodium-fluoride solutions are effective in children, but there is little evidence that such treatment is valuable after about the age of 15. The patient's consumption of refined sugar should be reduced and the calories lost should be replaced in detergent foods such as raw fruit and vegetables, preferably taken at the end of meals. This is effective in all but a small proportion of specially susceptible cases. A rational tooth-brushing technique must be taught and not merely demonstrated, and must be used after meals if possible; when this is impossible, rinsing should be substituted. Dental treatment should also include thorough polishing of the teeth several times a year. Painting with silver nitrate to disclose and arrest incipient caries before cavitation has begun may be classed as preventive or as curative treatment.

It is unfortunate that your correspondent cannot simply be told to refer his patients to a dental surgeon, but preventive dentistry will not develop until the public and the medical profession demand it, and it must somehow be made more profitable to the dentist than surgical and mechanical dentistry. Let us hope that the bureaucratic methods of the school dental service with its "output" of fillings and extractions (in the ratio of 100:180) do not foreshadow those of the brave new Health Service. The proposed introduction of hygienists suggests, rather, that the more preventive outlook of our American colleagues and the R.A.F. dental branch will be adopted.

Judicial Hanging.—Dr. J. R. V. FOXTON (New Norfolk, Tasmania) writes: I was interested in the answer to the question on the above subject (July 26, p. 160) and in the comments of Col. Rutherford (Aug. 16, p. 282). When a student at the Melbourne University, I attended a lecture on judicial hanging given by Prof. Frederic Wood Jones to a combined meeting of the Medical Students' Society and the Law Students' Society. If my memory serves me correctly he stated that the placing of the knot at the angle of the jaw (as is, I believe, the custom in British countries) rarely, if ever, fractures or dislocates the vertebral column, and death in judicial hanging occurs from strangulation or from fracture of the base of the skull. In either case consciousness may be retained for some time and death occurs slowly and painfully. He further stated that invariable fracture or dislocation of the cervical spine could only be obtained (*a*) by employing a very long drop, approximately that required to produce decapitation, or (*b*) by the placing of the knot under the chin, in which position it must be retained by some mechanical appliance. It would appear that judicial hanging as practised is an unnecessarily cruel and barbarous form of execution, and that reform is long overdue.

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